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FOREWORD

The advances in medical knowledge have been phenomenal during the past two decades. This has led to many changes in attitudes toward medical education at all levels, and to corresponding changes in teaching methods. Under present conditions it would be futile to attempt to impart encyclopedic knowledge to the student of medicine. So it is that present day teaching stresses the development of tricks of thinking and habits of study that will last for a lifetime. Only in this way may it be hoped that health scientists of all kinds will stay abreast of the wave of knowledge. Indeed, only in this way will it be possible for that wave to grow and to move unbroken.

These facts imply that medical men must communicate their observations, one to another. For

that purpose, there is no method to equal medical journalism.

The American Surgeon has long been distinguished as one of America's most effective instruments of communication. By its very creed, it is dedicated to "the advancement of surgery."

Here at Georgetown University School of Medicine, the members of the faculty feel strongly their obligation to contribute their full share to education by communication. The Department of Surgery, in particular the surgeons and their collaborators who have prepared the essays for this Georgetown number, are grateful to *The American Surgeon* for making it possible to fulfill that obligation in part.

HUGH H. HUSSEY, M.D., *Dean*

SUPRACONDYLOID PROCESS

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The supracondyloid process is a remarkable, constant osseous prong about 2 to 20 mm. in length which curves distally and projects from the anteromedial surface of the humerus about 5 cm. above the median epicondyle. It gives rise to a fibrous band which is attached to the epicondyle and from which the pronator teres muscle takes origin and into which fibers of the coracobrachialis muscle may insert. An arch is formed through which the median nerve and at times an undivided brachial artery or ulnar branch of a high dividing brachial artery deviate. The venae comitantes follow the deviated artery. The supracondyloid process is the phylogenetic survival of the structures about the supracondylar foramen found in many primate mammals and marsupials. In the human it is transmitted as a dominant hereditary trait.¹⁴

REVIEW OF LITERATURE

Friedrich Tiedeman, the German zoologist,^{20, 21} studied the occurrence of the supracondyloid foramen reporting its occurrence in 1818 and in 1819 in the ape and the monkey, and in 1822 he published an illustration of what he referred to as "an unusual excrescence of the humerus." To this he attached no significance. Knox⁷ predicted the occurrence of the supracondylar process in the human, in 1841, after studying the extremity anatomy of an American panther. He observed a definite groove in the cat's humerus and compared this with the human specimens in his laboratory. His prediction was soon confirmed in the dissected arm of a stout, middle-aged male cadaver. It was in 1854 that Struthers^{12, 13} collected 15 cases, including Tiedeman's recorded specimen. He presented a description of the anatomy of the process

and a review of the comparative anatomy. Several publications of the late 18th century indicated that the process was a common occurrence among mental defectives;^{5, 11} however, Cady² reported that the process was not more frequent in a group of 1000 defective people than in a normal group. In an extensive survey, Terry¹⁴⁻¹⁸ found only 1 case, with a process, to have a pathologic personality. Lund⁸ reported a case in 1930 with fracture of the process with median nerve numbness and forearm weakness which had been treated successfully with immobilization. Doane⁴ reported 2 cases with fracture of the process; one healed without treatment, the other required surgical excision. Mandruzzato⁹ reported 5 cases in 1938; two were subjected to surgery because of median nerve pain. In his case 4 he demonstrated a close relationship of the median nerve lying in a fibrous tunnel and the insertion of the pronator teres muscle and case 5 revealed an old fracture of the bony process. Symptom relief was obtained in cases 4 and 5 by complete excision of the bony process. Barnard and McCoy¹ reported 3 cases in 1946; one patient had no symptoms; another had symptoms with relief by rest and heat; the third had median nerve pain and was subjected to surgery with excision of the process, with a successful result. Witt²² reported 2 cases. One required excision because of pain and swelling about a unilateral process; the other, in a young child, was asymptomatic and required no treatment. Marquis and associates¹¹ reported 3 asymptomatic cases with radiologic evidence of the bony anomaly.

Incidence

In an anatomic monograph printed in 1859, Gruber⁶ noted the occurrence of the process in 2.7 per cent of his specimens. Testut,¹⁹ in his laboratory at Lyon, in 1889, studied 929 cadavers and found the anomaly 9 times, for an incidence of 1 per cent. More recently, Terry^{15, 18} found 1 in 1000 Negroes and 6 in 515 whites. This and subsequent work led him, along with others,¹²⁻¹⁴

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to conclude that there was an unusual racial incidence among people of European stock. In a survey of the osteologic material available in the anatomic laboratory at Georgetown University Medical School, 5 specimens among 348 humeruses examined were found to have a supracondyloid process.

Tiedeman^{20, 21} considered the anomaly to be a pathologic exostosis. This concept prevailed until anatomists by comparative studies on lower primates and marsupials showed the process to be related to the development of the supracondylar foramen. Struthers^{12, 13} demonstrated its development in the cat and proved it to be an anatomic variant. He showed that the theory of muscle pull at an insertion could not explain its occurrence

because the process was noted without muscle attachment. Struthers further noted in his dissections on kittens, ossification from a primary diaphyseal center. Cunningham³ found it in a full term stillborn infant, as did Terry. This, too, would seem to indicate that traction was not related to its occurrence. In the newborn examined by Cunningham the process was ossified from base to tip.

CASE REPORTS

Case I. V. H., a 38-year-old right handed painter presented for examination complaining of numbness in the median nerve distribution of the right hand and pain with wrist motion. Examination revealed tenderness, induration with crepitus of the flexor tendons at the wrist. Slight flattening of the right thenar eminence was noted. Roent-



Fig. 1 (Case 1). Roentgenograms of a supracondyloid process illustrating that a moderate degree of internal rotation of the humerus best demonstrated the process in this patient. Note the downward arch formed by the atavistic bony process.

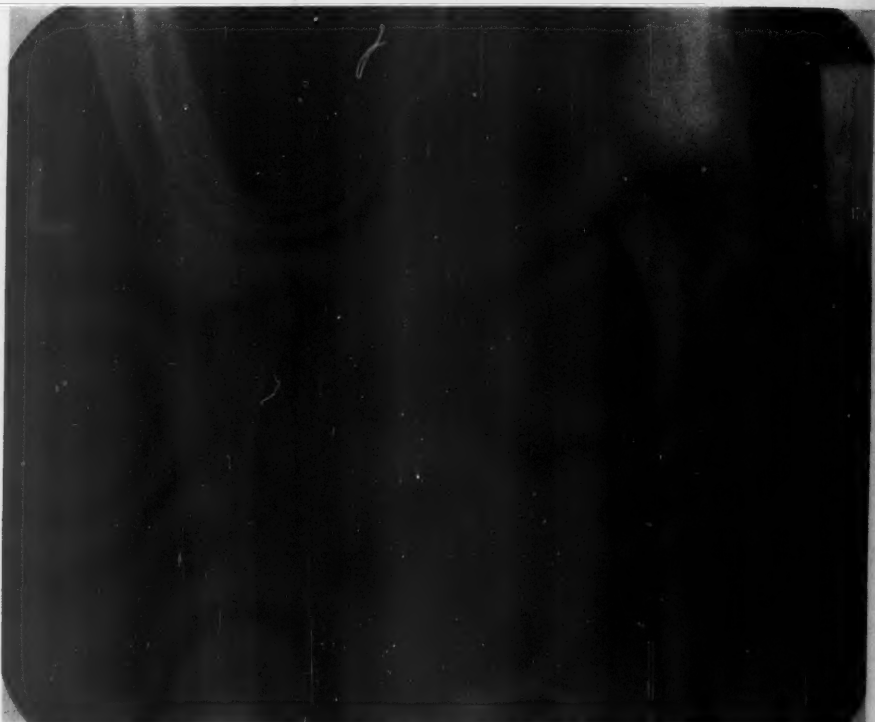


FIG. 2 (Case 2). Bilateral supracondylar processes are noted in the anteroposterior roentgenograms of both humeri.

genograms revealed a supracondylar process (fig. 1). Further examination revealed a supple cervical spine, symmetric shoulder and arm and forearm musculature. A diagnosis of tenosynovitis with presumptive carpal tunnel compression of the median nerve was made. The patient refused surgery.

Case 2. J. L., a 72-year-old retired colored man had been followed for several years with the diagnosis of generalized reticulum cell sarcoma. At follow-up he complained of a hard epitrochlear lymph node. Roentgenograms revealed bilateral supracondylar processes (fig. 2). One radiologist erroneously suggested the diagnosis of osteochondroma.

Case 3. H. B., a 28-year-old physician noted bilateral bony protuberances above the medial aspect of each elbow. Roentgenograms revealed bilateral supracondylar processes (fig. 3).

Case 4. P. A., an 18-year-old secretary complained of a deep ache above the lateral aspect of her right elbow. Roentgenograms revealed a supra-

condylar process. A diagnosis of tennis elbow was made. Symptoms regressed with heat and rest.

Case 5. C. E., a 9-year-old boy was thrown from his bicycle and sustained an injury to his right shoulder. An incidental finding of supracondylar process was reported by the radiologist.

Case 6. M. H., an 8-year-old male injured his left elbow playing football. A supracondylar process was noted by the radiologist.

Case 7. W. S., a 65-year-old insurance salesman was examined by his family physician who palpated a bony projection above the medial epicondyle of the left humerus. Roentgenograms revealed an asymptomatic supracondylar process.

Case 8. L. F., a 50-year-old housewife was involved in an auto accident. Roentgenograms of the elbows revealed a supracondylar process of the right humerus without symptoms.

Case 9. T. R., a 10-year-old boy noted a small asymptomatic bump protruding from the medial humerus just above the right elbow. Roentgeno-

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FIG. 3 (Case 3). Bilateral supracondyloid processes were found in this patient. Note the roentgenogram of the right elbow in the anteroposterior and lateral position. The process is well seen in both views.

grams revealed a supracondylar process (fig. 4A and B).

DISCUSSION

The diagnosis of supracondylar process is correctly made only when there is an awareness of its existence. Often the diagnosis of osteochondroma is made in error. In our experience 3 cases presented themselves for unrelated study and the diagnosis was made because there existed a high index of suspicion among our radiologists. The usual anteroposterior roentgenographic views of

the elbow missed the profile of the process in 7 of 9 cases. Lateral views failed to demonstrate the process adequately in 5 of 9 cases. It has been our experience that oblique roentgenograms of the distal humerus best showed the process. Oblique roentgenograms are obtained by taking an anteroposterior view with the arm in moderate internal rotation.

The clinical picture of supracondylar process can be varied. The process in most instances is an interesting and unusual finding. It is not usually



FIG. 4A (Case 9). A supracondyloid process is noted in the lateral roentgenogram but to a much less extent in the anteroposterior view.

related to symptoms. Only reassurance of the benign nature of the lesion need be given the patient. Those who present with symptoms of pain about the elbow in the absence of a history of trauma require a search for the etiology of the pain. Examination must exactly localize the site of pain. Roentgenograms of the radiohumeral and ulnohumeral articulations in several views must be made. Symptoms about the elbow in the absence of trauma are usually caused by tendinitis, bursitis, synovitis, arthritis or an old undiagnosed fracture. Excision of the process is not indicated. Occasionally the patient may present with a fracture of the process. This fracture usually is the result of a fall upon the affected elbow. Median nerve symptoms may appear early with the initial injury or later as the fracture heals with its or-

ganization of callus. In all fractures, except a small chip fracture of the tip of the process, total excision to protect the median nerve is indicated. Another group of patients with median nerve paresthesias in the hand and perhaps atrophy of the thenar eminence may have roentgenographic evidence of a supracondyloid process. These patients obviously have median nerve irritation and the exact level must be determined. Evaluation of the total musculature of the extremity must be done to determine whether there exists a pattern of atrophy or fasciculations. The diagnosis of a traction palsy secondary to a supracondylar process must be made with caution because the true etiology of the neurologic deficit may be found in the spinal cord, the cervical vertebrae, the bra-

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FIG. 4B (Case 9). Note the process is better demonstrated in full profile with an oblique view.

chial plexus or at the wrist. Once the diagnosis of traction palsy is made, total excision is indicated.

SUMMARY

1. The supracondyloid process is a small osseous prong situated on the anteromedial surface of the distal humerus forming an arch through which the median nerve deviates.

2. Roentgenographic examination of the elbow

in oblique views demonstrate the profile of the process best.

3. The process seldom gives rise to symptoms.

4. Total excision is indicated in fractures except small chips of the tip of the process and when there is definite evidence of a traction palsy of the median nerve at the proper level.

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USE OF FIVE PER CENT DEXTROSE IN WATER WITH CITRATED BLOOD*

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For many years, it has been considered undesirable to allow solutions of 5 per cent dextrose in water to come in contact with citrated blood during transfusion. Hemolysis of the transfused cells is alleged to occur; however, one of the authors (T. F. McD.) for several years has violated this tradition during transfusion on patients undergoing cardiac surgery, especially where sodium restriction was highly desirable. Although extreme clumping of cells was unsightly in the tubing through which blood was administered and tended to reduce the flow rate, particularly through small bored needles, no adverse reaction seemed to be encountered. This led to a study to determine the basis for this widely held belief. As part of the study, a search of the literature was made and certain clinical studies were carried out.

In 1950 Wilson⁷ described an elderly patient who had a kidney removed for unilateral disease and postoperatively received an intravenous drip of glucose into which blood was administered. Sudden chest and lumbar pains and shock appeared. This was thought to be due to the clumping of red cells in glucose which the authors demonstrated *in vitro*, a phenomenon reversible in saline and in alkaline solutions. No examination was made as to hemolysis in either the patient or the specimens.

In 1952 Watson and Pearce⁸ described a married housewife, 37 years old, who was subjected to uterine curettage for an incomplete abortion. As supportive measure, an intravenous drip of 5 per cent glucose in water was started in the operating room and, following the return of the patient to her bed, a transfusion of whole blood was given through the same tubing. The symptoms which followed the entry of this mixture into the vein included a chill, nausea and collapse associated with hypotension, rapid and weak heart action and an elevation of the temperature to 101.2°. After the discontinuation of this mixture, an infusion of normal saline solution was started. To

this, blood was added and the transfusion was completed without further mishap. The authors stated that agglutination of the erythrocytes occurs when citrated blood is mixed with aqueous solutions of glucose and concluded that this might be a cause of transfusion reaction. They recommended that glucose and water not be used as a medium for the administration of whole blood, packed or suspended red blood cells, or be introduced into tubing containing blood immediately before such a transfusion.

In 1953 Buschle and Saklad² developed a compatible solution for administration with blood. They examined various solutions of glucose and saline for clumping in the presence of transfused blood and found that 5 per cent dextrose and 0.09 per cent saline was satisfactory and recommended this as a routine solution to be given to patients before receiving blood transfusions. They later revised their recommended strength of saline to 0.11 per cent.⁵ They point out that this solution gives the postoperative patient better caloric source but not enough saline to be dangerous.

Ebaugh and associates,⁴ in 1958, mentioned but did not describe a series of hemolytic transfusion reactions following the use of secondary units containing 5 per cent dextrose and 0.225 per cent saline. They presented a paper at the International Hematologic Congress in Rome in 1958, and reported that the 10-minute *in vivo* survival of red blood cells exposed to 5 per cent glucose in 0.225 per cent saline for more than 30 minutes decreased rapidly to 10 per cent after 120 minutes *in vitro* exposure. This exposure is accompanied by progressive increase of red cell volume to a maximum of 180 per cent over this period of time accompanied by a marked increase of intracellular glucose due to osmotic effect. Red cells which have increased more than 150 per cent of original volume are said to be incapable of normal survival *in vivo*.

MATERIALS AND METHODS

The lack of cohesive evidence regarding hemolysis following 5 per cent dextrose in water encouraged us to undertake certain studies. In this

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institution, citrated whole blood as needed is given through a Y-set through which 5 per cent glucose in water solution is running to maintain the patency of the needle. Here, the citrated blood comes into limited contact with 5 per cent dextrose in water but produces visible clumping in the tubing. Secondary units, where extensive mixing may take place, are never used.

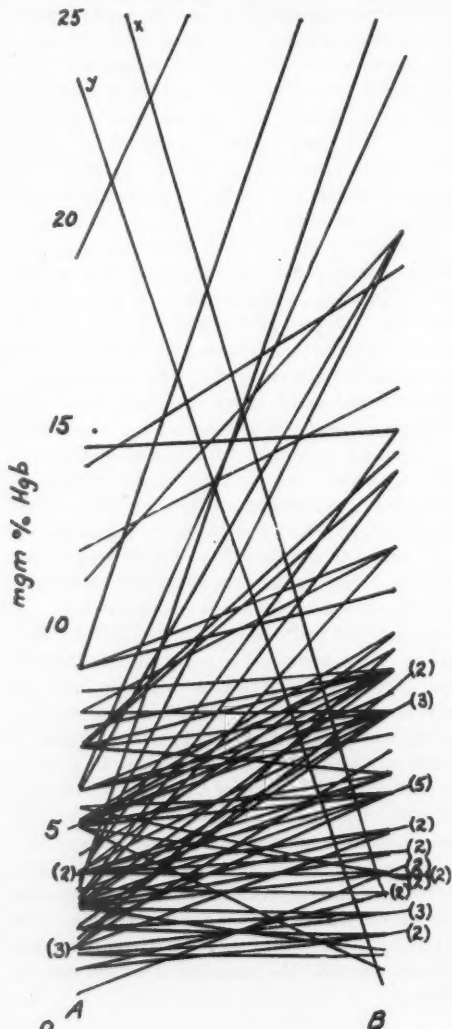


FIG. 1. Serum hemoglobin levels before (A) and after (B) transfusion of citrated blood which followed administration of 5 per cent dextrose in water. Figures in parentheses are duplicated results. For "X" and "Y," see text.

On 100 patients, all of whom had major surgery, a sample of blood was drawn before infusion of 5 per cent dextrose in water was started, and a second sample of blood was drawn just after the completion of transfusion. The serum hemoglobin in both the samples was determined by Crosby and Damesheks' modification of Bing and Bakers^{21, 23} benzidine method. Of these patients, 60 were women and 40 were men. Their ages ranged from 3 to 79 years, averaging 47.7. The amount of blood given ranged from 1 to 9 pints. A control study was made on 25 cases where only 5 per cent glucose in water was given with samples taken before and after infusion.

Consideration of the findings obtained from the study group of 100 patients indicates the technical difficulties of obtaining 200 consecutive blood samples and analyzing them for serum hemoglobin without serious technical error occasionally creeping in (fig. 1). A sharp fall in serum hemoglobin as seen in cases X and Y in this figure cannot be accounted for in any other fashion. Then, too, none of the initially high values were accounted for by the patient's clinical condition. We can then only speculate on errors in the post-transfusion specimens.

To minimize this distortion, it was decided to select at random 25 of the transfusion cases whose initial value fell between 2 and 10 mg. of serum hemoglobin per 100 cc. and compare these with the 25 control cases (whose initial values also fell between 2 and 10 mg. per 100 cc.). The upper limit of normal is considered to be 15 mg. of serum hemoglobin per 100 cc. A rise of less than 8 mg. per 100 cc. is not considered clinically significant.

The findings for the control cases are shown in figure 2 and for the random selected transfusion cases, in figure 3. When subjected to statistic analysis, the mean difference in pre- and postinfusion samples in the control group was 1.52 ± 3.25 mg. per 100 cc., while the mean difference between pre- and posttransfusion samples was 2.8 ± 3.9 mg. per 100 cc. Calculation of the significance between these means according to Fisher's T-test reveals that $p = 0.2$, and, therefore, there is no significant difference between these groups. To state this more simply, blood transfused in the described fashion does not reveal an amount of hemolysis in excess of that observed with infusion of 5 per cent dextrose in water alone.

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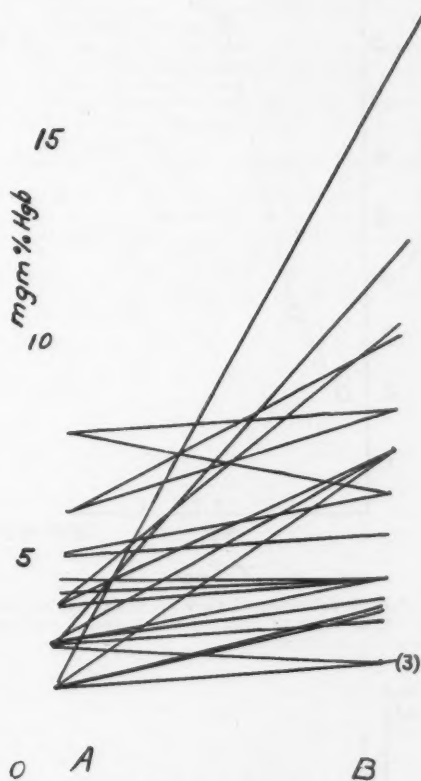
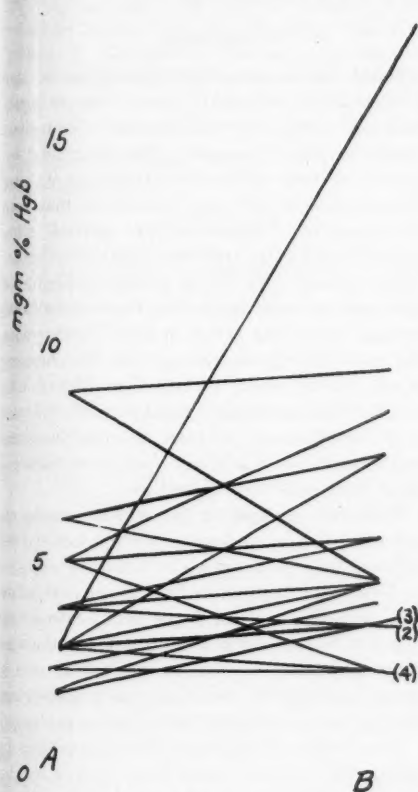


FIG. 2. Control series of serum hemoglobin levels before (A) and after (B) infusion of only 5 per cent dextrose in water during surgery. Figures in parentheses are duplicated results.

FIG. 3. Serum hemoglobin levels in 25 patients with initial hemoglobin levels between 2 and 10 mg. per 100 cc., selected at random from the data in figure 1, before (A) and after (B) transfusion of citrated blood which followed administration of 5 per cent dextrose in water. Figures in parentheses are duplicated results.

Experiments in Vitro

1. *Influence of time on hemolysis.* Equal amounts of blood and 5 per cent glucose in water in different samples were mixed and exposed at room temperature for various lengths of time from 15 to 120 minutes and then the hemolysis of each sample was determined. The longer the blood was exposed to 5 per cent glucose in water, the more hemolysis occurred. Hemolysis accelerated most rapidly during the second half-hour interval but did not exceed 11 mg. per 100 cc. even after 2 hours' exposure (fig. 4).

2. *Influence of dilution on hemolysis.* Equal quantities of blood were mixed with varying

quantities of 5 per cent dextrose in water at room temperature and hemolysis was determined after 30 minutes. The amount of free hemoglobin found declined progressively with increasing dilution of the blood, but never exceeded 9.5 mg. per 100 cc. in any case. When viewed in terms of percentage of available hemoglobin hemolyzed, the maximum observed was but 0.19 per cent (fig. 5).

3. *Reversibility of red cell agglutination due to 5 per cent glucose in water solutions.* Red cells were suspended in 5 per cent glucose solution and large clumps were seen under the microscope. The re-

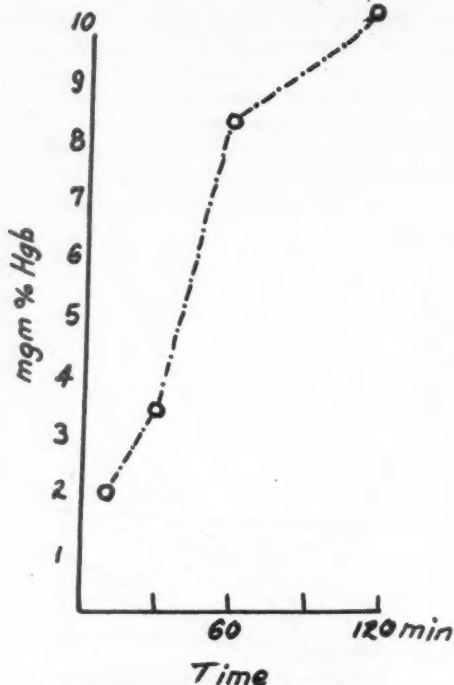


FIG. 4. Influence of time on hemolysis *in vitro* of equal parts of citrated blood and 5 per cent dextrose in water.

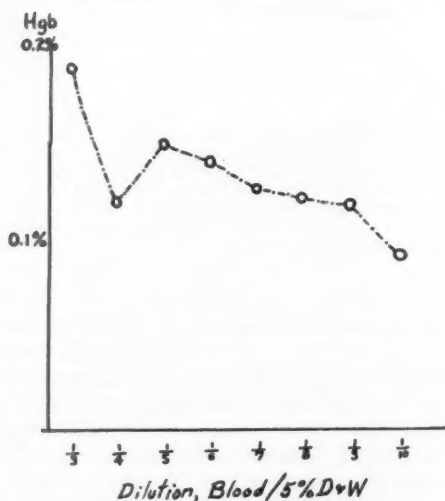


FIG. 5. Percentage of hemolysis of available hemoglobin in citrated blood in various dilutions with 5 per cent dextrose in water.

versibility of this agglutination was proved by replacement of the dextrose solution by saline 0.85 per cent. The clumps were broken down and free red cells were observed.

DISCUSSION

The studies *in vitro* above indicate that mixture of blood and 5 per cent dextrose in water is productive of a relatively small amount of immediate hemolysis which increases after prolonged exposure, but does not become excessive even after 2 hours. This would seem to indicate that from the viewpoint of hemolysis, any method of following 5 per cent dextrose and water with citrated blood is acceptable where mixing is kept at a minimum and where such a mixture is not allowed to stand for a long period of time. Furthermore, the probability is very strong that the clumping of red cells so readily reversed by dilution with normal saline is probably equally readily reversed in the blood stream. At least, no evidence of embolic phenomena was observed either in this series or previous extensive clinical use.

This sheds no light on the very interesting observation of Ebaugh and associates⁴ that red cell survival may be poor *in vivo* following exposure to 5 per cent dextrose and 0.225 per cent saline. One would not expect 5 per cent dextrose and water to be superior in this respect, but the reactions mentioned by these authors were said to occur following the use of *secondary* units where mixing may be extensive and exposure prolonged.

It is further interesting to note that even in our cases with high post-transfusion levels of free hemoglobin, there appeared to be no clinical morbidity detected.

SUMMARY

Twenty-five cases, whose initial level of hemolysis was within 2 to 10 mg. per 100 cc., picked at random from the 100 cases done, were statistically compared with the 25 control cases who received 5 per cent dextrose in water only and showed no significant difference in hemolysis between these two groups.

In vitro experiments exposing blood to 5 per cent glucose in water increased hemolysis in 20 minutes but not until after 10 minutes. Clumping of red blood cells in 5 per cent glucose in water is reversible in normal saline.

The amount of free hemoglobin found in the mixture of blood and different dilutions of 5 per

cent dextrose in water declined progressively with increasing dilution of blood.

Acknowledgment. The authors wish to acknowledge the assistance of John C. Houck, Ph.D., Director of the Surgical Research Metabolic Laboratory, Georgetown University Medical Center, for his aid in interpretation of our statistical data.

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REFLUX ESOPHAGITIS

MODALITIES IN SURGICAL THERAPY: SUBTOTAL GASTRECTOMY: RIGHT COLON INTERPOSITION*

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During the past year we have encountered serious complications in two patients with reflux esophagitis. One patient suffered from persistent bleeding, and later massive bleeding, from an eroded lower esophagus; this problem has been controlled in part by performing subtotal gastrectomy. The other patient had severe and persistent stenosis of the lower one-half of the esophagus with complete destruction of mucosa and extensive fibrosis; this problem was managed by connecting the upper esophagus to the stomach, using the right colon for the bypass.

There is, as yet, no unanimity of opinion as to the best method of managing serious reflux esophagitis. Accordingly, we thought it might be of interest to report our recent experiences and to review some of the important considerations relating to this disease.

Lyall¹ described two types of esophageal ulceration; one a diffuse superficial inflammation with patches of healing intermingled with more chronic, deeper erosions; the other a circumscribed deep ulcer. Barrett¹ also noted that the more common lesion is an erosion of the squamous epithelium of the lower esophagus which encircles the lumen and bleeds easily. Active ulcerations are seen side-by-side with ulcers which are shallow and healing. The affected segment may be from 1 to 8 cm. in length.

"Gastric ulcer" may occur in the lower esophagus, developing in ectopic gastric mucosa. These ulcers are usually single, tend to spread longitudinally rather than encircle, and are apt to be penetrating. Hemorrhage or perforation is more apt to be a complicating factor of such gastric ulcers than is stenosis. Peptic erosion with stenosis and gastric ulcer may be seen together in the lower segment of the esophagus in some patients.

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Reflux esophagitis may be of any degree of severity; there may be mild erythema, hemorrhagic erythema, ulceration or cicatrization and stenosis. An arbitrary classification of grades 1 through 4 may be made, depending on the degree of injury.

Esophagitis has been reported in 7 per cent of autopsies. McHardy and associates² report an incidence of 5.8 per 1000 hospital admissions.

CLINICAL FEATURES

Esophagitis causes pain which is usually substernal or high epigastric, often burning in character (pyrosis) but may be sharp and radiate to the neck, jaw, left arm or back. Pain may be initiated by bending forward, lying down or by a sudden increase in intraabdominal pressure. Patients often regurgitate gastric contents. The symptoms may be relieved by standing, or by taking milk or alkali. Patients are more comfortable when the stomach is empty and hence may have "food fear" and weight loss.

Other features include dysphagia, which may be due to mild spasm or true obstruction, bleeding, usually leading to insidious anemia but sometimes massive hemorrhage, dyspnea and cough. Symptoms may be of short duration or may have been present for years. As with duodenal ulcer, there may be periodicity of symptoms.

Examination of patients with suspected esophagitis should include a complete history and physical and in addition an upper gastrointestinal x-ray, cholecystogram, and an electrocardiogram. In addition, all patients must be esophagoscoped so as to definitely establish the diagnosis and also to estimate the degree of stenosis, the degree of fixation of the esophagocardiac junction, and also to rule out possible concomitant carcinoma.

ETIOLOGY

Several etiologic factors probably combine to produce reflux esophagitis. As the name implies, an important factor is the presence of stomach,

duodenal or jejunal secretions in the lower esophagus. Inasmuch as the disease may complicate esophagojejunal anastomosis following total gastrectomy, it is apparent that acid-pepsin is not the only irritant to the squamous cell epithelium of the lower esophagus.

Perhaps the single most important etiologic factor is a defect in the esophagocardiac mechanism which permits reflux into the esophagus. Usually there is an associated sliding hiatal hernia and it is uncommon to find persistent peptic esophagitis without the presence of such a hernia.

Normally, the esophagocardiac junction is kept closed by several mechanisms: the oblique angle of entry of esophagus into the stomach; a weak sphincter muscle in the lower esophageal wall; the sling-like pull of the right crus of the diaphragm which, on inspiration, tends to pinch off the opening; the gas bubble elevating the fundus of the stomach and the anchoring effect of the left gastric artery.

The esophagocardiac sphincter is often incompetent with sliding hiatal hernia. It is destroyed, damaged or bypassed by several surgical procedures designed to alleviate other conditions, e.g., following esophagogastric resection, esophagocardioplasty or myotomy, and following lateral anastomosis of the esophagus to the fundus of the stomach.

Prolonged vomiting may lead to esophagitis as seen on a psychogenic basis, in alcoholism, in hyperemesis gravidarum and with chronic pyloric or duodenal obstruction.

Severe esophagitis may follow acute relaxation of the cardioesophageal sphincter as may occur under general anesthesia, or with patients in labor when anesthesia is given. It may be associated with the use of an inlying nasogastric tube. Gastroduodenal ulcer diathesis is frequently associated with reflux esophagitis.

Reflux of acid-pepsin can occur in the absence of hiatus hernia and more importantly, reflux is not always associated with the development of serious esophagitis. There is probably a factor of individual susceptibility perhaps related to the efficacy of protection against or neutralization of intestinal juices by saliva or esophageal secretions.

Sometimes the lower esophagus is lined by ectopic gastric mucosa which continually secretes gastric juice. In infants and children the resultant

peptic esophagitis is followed by stenosis and shortening causing the true short esophagus.¹

TREATMENT

Medical measures will control reflux esophagitis in most patients. These include sleeping in the semi-Fowler position, taking several small bland feedings each day, taking alkali by mouth every 2 hours, and taking antispasmodics and sedatives. Bouginage may be necessary if stenosis is present, but Sweet and co-workers¹⁰ have stated that once the mucous membrane is completely destroyed around the entire circumference of the esophagus improvement from dilation is usually transitory.

Surgery is reserved for the complications of reflux esophagitis, as is true with duodenal ulcer; if the disease is progressing in the face of medical treatment then surgery must be done. The common indications are dysphagia due to stenosis, and hemorrhage due to erosion. Other indications for surgery are intractable pain or perforation. There may be combinations of these factors in any one patient. It is important to indicate to the patient that even though surgery is necessary, medical measures are often necessary postoperatively.

The objectives of a surgical approach are: to prevent reflux of gastric juice, to reduce gastric acidity, to provide adequate drainage of the gastric reservoir and to relieve stenosis of the lower esophagus if present. Several operative procedures have been advocated. For esophagitis in the absence of stenosis, the following have been recommended:

1. Reduction and repair of the hiatus hernia
 2. Vagotomy and gastroenterostomy
 3. Vagotomy and antrectomy
 4. Subtotal gastrectomy
 5. Finney pyloroplasty
 6. Paralysis of the left leaf of diaphragm
 7. Interposition of a jejunal or colon segment between esophagus and stomach
 8. Various combinations of the above.
- If stenosis is present, additional suggested procedures include:
9. Lateral anastomosis between esophagus and fundus of stomach, above the stricture, combined with vagotomy and pyloroplasty
 10. Esophagogastric resection plus pyloroplasty
 11. Resection of the stricture and interposition of

a segment of jejunum or colon plus vagotomy and pyloroplasty

12. Subtotal gastrectomy plus postoperative bouginage
13. Longitudinal division of the stricture with re-suture transversely.

The following 2 cases demonstrate some of the features of reflux esophagitis. The predominant complication was different in each case and therefore the definitive surgical approach differed.

CASE REPORTS

Case 1. A 68-year-old Negro woman was admitted to the Georgetown University Surgical Division, District of Columbia General Hospital, with the chief complaint of dysphagia, occasional vomiting and intolerance to fatty foods. The symptoms were slowly progressive and had been present for years. Diagnostic studies revealed achalasia of the esophagus and routine chest x-ray showed a gas- and fluid-filled organ occupying the medial half of the right hemithorax. A barium swallow showed a huge tortuous esophagus partially filled with food residuals (fig. 1). Esophagoscopy confirmed the diagnosis of megaesophagus and ruled out concomitant carcinoma. There was no esophagitis. The hematocrit was 41 per cent.

The patient underwent a Heller-type esophagogastric myotomy successfully with clinical and x-ray improvement of dysphagia (fig. 2). Eleven



FIG. 1. Case 1, before pyloromyotomy

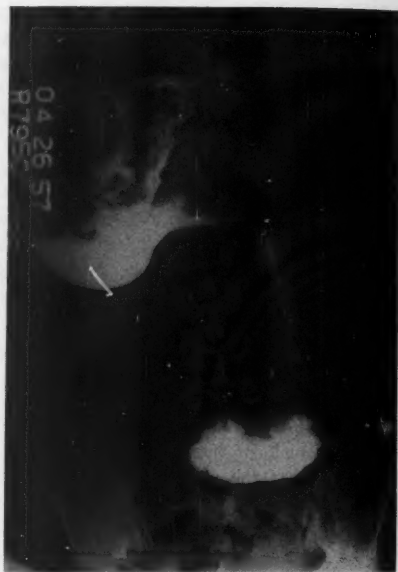


FIG. 2. Case 1, after pyloromyotomy

months after surgery the patient began to complain of dizziness, weakness and anorexia. Then she passed three tarry stools. On readmission to the hospital the hematocrit was 17 per cent. An extensive work-up failed to reveal the site of bleeding.

Esophagoscopy demonstrated the previously noted enlarged esophagus. There was no evidence of inflammation, but the esophagogastric junction was narrow and required dilation with bougies. A repeat barium swallow several days after symptomatic treatment revealed the rapid passage of barium through the cardioesophageal junction. Following blood transfusion and medical therapy, the patient appeared to stabilize and was discharged to the medical clinic for follow-up. However, anemia persisted and stools remained intermittently positive for occult blood. Repeated work-up failed to demonstrate the bleeding site.

Eighteen months after the original Heller operation the patient vomited "Coffee-ground" guaiac positive material for the first time. She became cold and clammy with a blood pressure of 94/55 and a pulse rate of 120 per minute. Esophagoscopy again failed to establish the bleeding site. An emergency laparotomy was done when the patient failed to stabilize after blood transfusions (4500 cc). Abdominal exploration was negative. Portal pressure was 160 mm. of saline. A high gastrotomy revealed blood entering the stomach through the gastroesophageal opening.

The abdominal incision was extended into the left thoracic cavity and the lower esophagus examined. Erosion and bleeding of the mucosa at the gastroesophageal junction was visualized. The esophagus appeared normal otherwise except for the presence of megaesophagus. Definitive treatment consisted of a high subtotal gastrectomy and gastrojejunostomy (Hoffmeister). The postoperative course was uneventful. The patient did well thereafter for 12 months except for a 20-lb. weight loss. At the end of this period of freedom from hemorrhage, she again bled suddenly from the upper intestinal tract. At esophagoscopy a single bleeding varix was seen in the midesophagus. No recurrence of esophagitis was noted nor were there other varices. The patient responded to conservative management but the follow-up period is short.

Comment. This is an example of reflux esophagitis with complicating hemorrhage which followed surgical destruction of the cardioesophageal sphincter. The Heller procedure for the relief of megaesophagus consists of the longitudinal division of all muscle layers at the esophagocardiac junction. This permits swallowed content within the atonic esophagus to pass easily into the stomach. It also permits the gastric contents to regurgitate easily into the esophagus. For this reason the Heller procedure should always be accompanied by a distal stomach drainage procedure (pyloroplasty). Subtotal gastrectomy and gastrojejunostomy appear to have prevented further significant reflux in the above patient. Bleeding ceased for 12 months even though the bleeding site was not attacked directly. The recurrent episode of bleeding 1 year after gastrectomy was thought to be from a varix in the midesophagus. At the time of subtotal gastrectomy the portal pressure was normal. Vagotomy was not done because of the amount of periesophageal scarring present.

Case 2. A 15-year-old Negro girl was first admitted to the District of Columbia General Hospital in 1954, in the 38th week of her first pregnancy, suffering from severe eclampsia. On the 2nd hospital day she vomited guaiac positive material but no previous vomiting had occurred. A low cervical cesarean section was done because of disproportion and toxemia. Her immediate convalescence was uneventful except that the patient complained of sore throat and difficulty in swallowing. She was readmitted to the hospital 3 months later with the diagnosis of acute tonsillitis. A barium swallow was done because of com-

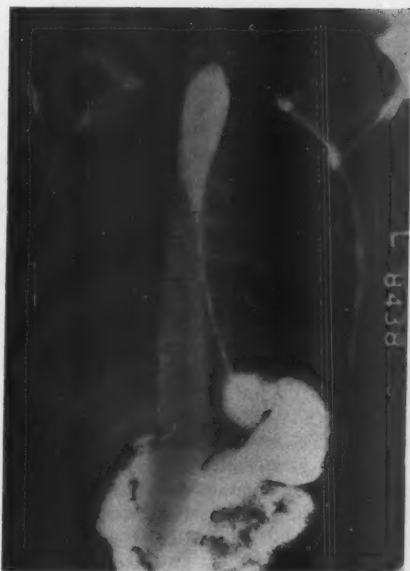


FIG. 3. Case 2, pregastrectomy



FIG. 4. Case 2, pregastrectomy

plaints of dysphagia but was reported as normal. The difficulty in swallowing persisted after discharge from the hospital and 7 months later she was readmitted because of inability to swallow liquids. There had been progressive weight loss.

Barium swallow (figs. 3 and 4) revealed an esophageal stricture which was confirmed by esophagoscopy. The stricture commenced 23 cm. from the incisor teeth. The stricture was dilated with bougies and the patient discharged from the hospital. She was readmitted to the hospital 3 times within the following 10 months for stricture dilation. A string would not pass on the 3rd admission so that retrograde dilation was required. This necessitated both gastrotomy and thoracotomy. At this time the patient was again pregnant and thereafter vomited frequently until a cesarean section was done. Bouginage of the stricture was done twice between the time of thoracotomy and cesarean section. The patient was readmitted to the hospital 7 times for stricture dilation within a 9-month period following cesarean section. On the last of those admissions her weight was 67 lb.

A bilateral vagotomy and subtotal gastrectomy (Pólya-type gastrojejunostomy) was then done almost 3 years after the onset of her esophageal difficulties. The esophageal stricture was dilated on the 10th and 24th post gastrectomy days and the patient discharged from the hospital apparently improved. Dilation was again required 5 and 7 months postgastrectomy (fig. 5). At that time the patient's weight was 63 lb.

An esophageal "bypass" operation was then done. The abdomen was opened through a long midline incision and the right chest through a standard right lateral thoracotomy incision. The



FIG. 5. Case 2, after subtotal gastrectomy



FIG. 6. Case 2, after right colon bypass

esophagus was transected immediately above the stricture in the upper one-third of the thorax. The distal esophagus was closed and left *in situ*. An appendectomy was done and then the terminal ileum, cecum, ascending colon and right one-half of the transverse colon were rotated up into the chest passing through the esophageal hiatus. The middle colic artery provided blood for the transposed segment. The terminal ileum was anastomosed to the proximal esophagus and the divided end of the transverse colon to the lesser curvature of the stomach (fig. 6). Lower intestinal tract continuity was reestablished by anastomosing the proximal end of divided ileum to the distal one-half of transverse colon. The postoperative course was uneventful. The follow-up period has been 10 months. There is no dysphagia. The patient eats an unrestricted diet. Her present weight is 98 lb. (35-lb. weight gain). A large meal causes some epigastric discomfort but otherwise the patient states that she is well.

Comment. This patient represents an example of reflux esophagitis with severe complicating stenosis. Vomiting late in pregnancy appears to have initiated the esophageal injury which was severe. Recurrent vomiting in the subsequent years increased the damage. Eventually the lower esophagus was entirely replaced by scar tissue.

The patient presented a particularly difficult problem in management in that she would not

submit to progressive esophageal dilation, nor would she accept dilation without general anesthesia. Each time she was discharged from the hospital she would not return to the clinic for continuing treatment until she was unable to swallow water.

Subtotal gastrectomy and gastrojejunostomy failed completely to relieve the situation even though bouginage was done postoperatively. This was because the esophageal destruction was complete and scar dilation was always followed by contraction. If the stricture had been due to edema and submucosal fibrosis, then gastric resection and bouginage might have been sufficient.

The colon bypass has worked very well to date. The patient is very pleased and has returned to a normal life. Erosion of the lower colon has not occurred so far as we know. However, the patient has a high gastrectomy with good gastric emptying so that reflux is probably minimal. She has not vomited since we inserted the bypass. The 35-lb. weight gain in our patient attests to the adequacy of the colon as a conduit for food when used as described.

DISCUSSION

The variety of surgical approaches to reflux esophagitis suggests that no one procedure is entirely satisfactory. If a hiatus hernia is present it (probably) should be repaired and if this is technically satisfactory and reflux prevented, nothing more need be done. If there is doubt about the control of reflux or if peptic ulcer diathesis is present, then in addition, an adequate drainage procedure should be done to the stomach (*e.g.*, vagotomy and gastrojejunostomy or Finney pyloroplasty) or a subtotal gastric resection may be added. Carver² does not think that subtotal gastrectomy alone is sufficient for esophagitis if a hiatus hernia is present. The latter must also be repaired. Fisher and Johnson,³ however, noted that subtotal gastrectomy alone was often followed by the return of the stomach to the abdomen, even though a hiatus hernia was present preoperatively.

If stenosis of the lower esophagus is present, some bypass operation must be done also. This necessitates the elimination of the esophago-gastric sphincter mechanism; therefore, gastric acidity and retention must be reduced also by vagotomy and a distal gastric drainage procedure (gastrojejunostomy or pyloroplasty) or gastric re-

section. MacLean and Wangenstein⁵ feel that even if stenosis is present, subtotal gastrectomy and bouginage of the esophagus may be the optimal procedure. This reduces gastric acidity and provides good distal drainage. Thus reflux is reduced and is less harmful and the bouginage can maintain esophageal dilation. This did not control the problem in our second case, however.

There are many advocates of esophagogastrectomy once stenosis has developed, but as Stewart and associates have noted,⁹ this operation is not ideal, for gastric acidity may not be abolished and the sphincter mechanism preventing reflux is crippled.

It is precisely for this reason that the jejunal and colon interposition operations have their advocates. Merendino and Dillard⁶ claim that jejunal mucosa (in dogs) is more resistant to acid-peptic digestion than is esophageal mucosa. Not only does the interposed jejunum provide a conduit for food by replacing the resected stenosed esophagus, but because it is isoperistaltic it is said to act as a sphincter substitute. A vagotomy and pyloroplasty must also be done, however. One disadvantage of jejunal interposition is that if a long segment is required there is real danger of necrosis of the proximal end because of inadequate blood supply.

Colon interposition⁶ has the advantage that a long segment with a good blood supply can be easily mobilized so that if the anastomosis to esophagus must be in the high thorax or neck the method is safer. We are impressed by the relative ease of this procedure and feel that it will prove to be the operation of choice for esophageal substitution in the upper thorax. Our own patient has had a remarkably benign course following right colon bypass.

SUMMARY

Current opinion regarding reflux esophagitis is reviewed. Diagnostic measures are outlined and medical and surgical therapy discussed. No one surgical procedure is universally accepted. Hiatus hernia, if present, should be corrected and at times gastric acidity should be decreased. Adequate gastric emptying must be assured. Severe esophageal stricture must be bypassed.

Two illustrative cases are presented.

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A FURTHER EVALUATION OF LYMPHEDEMA OF THE ARM FOLLOWING RADICAL MASTECTOMY AND POSTOPERATIVE X-RAY THERAPY

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Halsted¹² first described the clinical picture of lymphedema of the arm following mastectomy, calling it "elephantiasis chirurgica." He did much to stimulate interest in the underlying causes and problems surrounding this complication. He, himself, felt that bad wound healing with infection, following radical mastectomy, played a large role in producing lymphedema of the arm. In the last two decades there has been an increasing amount of investigation into the causes. Veal²¹ came to the conclusion that edema resulted from obstruction of the axillary and subclavian veins in a considerable number of such patients. He has observed an increase of venous pressure in the affected arm and has demonstrated the presence of venous obstruction by venography. Deaton and Bradshaw⁴ concluded from their clinical investigations that increased venous pressure does not seem to be an important factor. They incriminated excess scar tissue and infection as important background pathology in the development of arm edema. Russo and associates²⁵ reported studies in which changes in the axillary vein could be readily demonstrated. The variations extended from a mild distortion to a complete occlusion of the axillary vein. After a period of months, the alterations in the vein usually cleared up.

Devenish and Jessop^{5, 6} ascribed a major role in arm swelling to the interruption of the axillary lymphatics. Using dye injections, they demonstrated variations in lymph drainage between normal and abnormal upper extremities. They further pointed out that a greater number of lymphatics in an obese person are removed in the development of the superior skin flaps at operation, whereas, in a thin individual, a greater amount of fat is left on the flap, sparing the lymphatics. The result is a decreased incidence of lymphedema in the arms of thin patients. Deven-

ish and Jessop thus advocated leaving a sufficient thickness of subcutaneous tissue on the upper axillary skin flap in all cases to reduce the incidence of arm edema.

Haagensen¹¹ is convinced that infection is the underlying cause of postmastectomy arm edema. He has observed repeatedly that when edema of the arm develops, early treatment with the proper antibiotics, given within 1 to 7 days after onset, will result in a normal arm. Just how infection interferes with the lymphatic flow and produces edema is not clear, but Haagensen feels that if infection is treated early, the process is reversible but when the infection has been present for some time before using antibiotics, the treatment is usually not successful.

Other factors^{22, 30} which have been mentioned as causing or aggravating lymphedema are: poor location of the incision, angulation of the axillary vein, prolonged drainage, axillary or supraclavicular recrudescence of disease, large serum collections, obesity and changes brought about by postoperative x-ray therapy. MacDonald¹⁸ is convinced that obesity is the most important single factor in its genesis predisposing, as it does, to fat necrosis in the operative field.

The use of routine postoperative x-ray therapy following radical mastectomy for carcinoma of the breast has long been a controversial subject. In the Oncology Department of the Georgetown University Medical Center all patients with breast carcinoma who, at surgery, are found to have metastases to axillary lymph nodes are given a course of postoperative x-ray treatments to the axilla and chest wall. It is our belief that this regimen yields a higher percentage of 5- and 10-year survivals and reduces the local recrudescence of disease.

In recent years there has been a move by some to abandon radical mastectomy as the treatment of choice for breast carcinoma. McWhirter²¹ and others claim that better survival results are obtained by simple mastectomy, followed by postoperative irradiation. Although we still think that every patient with operable breast carcinoma

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should have the benefit of radical mastectomy, it is not our aim to discuss the surgical aspects but to consider the relation, if any, of postoperative irradiation to swelling of the arm following radical mastectomy.

Adair,¹ Oberhelman²³ and Bell² have reported an increased incidence of lymphedema of the arm following x-ray therapy. Oberhelman considered the cause to be excessive radiation fibrosis. Holman and associates,¹³ in a review of 100 cases, found that 70 cases had detectable swelling, whereas 11 per cent had "marked swelling." They concluded that the greatest factors in causing swelling were x-ray dermatitis and wound infection. Swelling was present in all 29 patients who had both x-ray treatment and infection, and all with marked swelling had both. Guthrie and Gagnon¹⁰ pointed out that roentgen therapy may precipitate chronic edema by blocking the lymphatics before collateral circulation takes place, favoring the formation of fibrosis. Edema, however, developed in only 8 of their 56 patients receiving x-ray therapy. Six of these patients showed a subsidence of edema with conservative therapy. Gratzek and Stenstrom⁹ stated that the relationship between arm edema and postoperative irradiation appeared to be controversial, noting the variation in reports on the incidence and the paucity of reliable data. Villazor and Lewison^{16, 32} have recently reported a survey by individual examination on two series of post-mastectomy patients, with and without arm swelling. A multiplicity of factors was considered in this study. The authors concluded that there was no determinant common denominator which could be held constantly responsible for the development of this condition. The factors which appeared to have some relationship were: wound infection, radiotherapy, axillary metastases, immobilization of the arm and injections into the affected arm. Infection and x-ray therapy were considered important factors in causing or aggravating existing edema, and x-ray therapy seemed related to a higher percentage of patients with severe lymphedema. Daland,³ in an important study of the subject, concluded that both x-ray therapy and radical surgical dissection were important factors in producing postoperative arm swelling.

In the operation of radical mastectomy, tenting of the skin over the axilla leads to dead space with collections of blood and serum which predis-

pose to infection, increases the amount of cicatrix formed and results in a greater possibility of angulation and/or occlusion of the axillary vein. Skin grafting, allowing better utilization of the lateral flap to obliterate dead space, is advocated by some to lessen the incidence of these complications. To prevent cicatrix forming about the axillary vein with angulation or obliteration of the vessel, various muscles have been used to cover the vein and help obliterate dead space. Rienhoff²⁴ utilized the latissimus dorsi but is quoted by Treves as having given up the method because he decided that it is of no value. Treves²⁵ has advocated the use of Gelfoam rolls to splint the vein, obliterate dead space and provide a "bridge" for the regeneration of lymphatics. All such procedures seem doomed to failure in a large percentage of cases.

We believe that the following measures will do much to prevent the development of edema: (1) careful placement of the incision, avoiding the axilla and arm; (2) gentle handling of tissues, with sharp, cold steel dissection; (3) the use of fine, nonabsorbable suture material to effect perfect hemostasis; and (4) the application of a bandage which will obliterate dead space, yet allow early mobilization of the arm without occluding the axillary vein. Additional factors which seem to be of value as prophylactic measures are: (5) carefully administered x-ray therapy to prevent excessive radiodermatitis; (6) the avoidance of injections or injury of any sort to the arm on the affected side; and (7) the prevention of even minor infections of the homolateral hand and arm. We have, for some time, used the method, originated by others, of inserting a multiperforated catheter into the axilla through a stab wound, and placing it on constant suction immediately postoperatively. The results, in terms of fewer serum collections, better adherence of flaps and wound healing, have been most gratifying.

A further analysis of our increasing clinical material has been made in an effort to reevaluate the role of postoperative x-ray therapy in the development of edema. In doing this we have again compared our results with Daland's series, few of whom received postoperative therapy. Daland studied 90 patients who had had radical mastectomy. Among these, 17 per cent had "moderate" swelling of the ipsilateral upper arm, an increase of from 2.5 to 4.5 cm., and 5.5 per cent had "severe" swelling with increase in circumference

of from 5 to 15 cm. An additional 31.0 per cent had slight swelling (less than 2 cm.). Arbitrarily selecting 2 cm. as a figure at or below which swelling is insignificant, we have determined, according to our classification, a significant swelling of the upper arm in 22.5 per cent of Daland's cases.

ANALYSIS OF DATA

Among 437 patients with breast carcinoma treated in the Oncology Department of the Georgetown University Medical Center since 1947, we have recorded the measurements of the affected and unaffected arms in 100 patients who have received a cycle of x-ray therapy to the axilla, following radical mastectomy. The majority of the patients (72) have been followed from 1 to 9 years following the completion of therapy. In 28 patients the follow-up period has been from 2 months to 1 year after the completion of treatment.

The quality of irradiation used is reflected in the following physical factors: 250 kv. roentgen rays, 1.9 mm. Cu half-value layer, 1 mm. Cu added filter and 1 mm. Al added filter. The target skin distance used was 50 cm. Approximately 2000 r of x-ray therapy were given to each of three axillary portals at the rate of 200 r per day, alternating between the three portals in rotation. On the average, a 10- by 10-cm. posterior axillary and anterior axillary port were used, in addition to a direct axilla circular portal 10 cm. in diameter. This results in a tumor dose approximating 4600 r at the center of the axilla, according to the anatomic measurements as described by Duffy and Lucas.³

There was no rigid uniformity of operative technique, which varied with the individual surgeon. The patients were sent for postoperative radiotherapy at various periods ranging from 10 days to several weeks after surgery.

In common with other reported series of breast cancer, 79 patients (79 per cent) had axillary metastases and of these, 53 (67.1 per cent) developed a swollen arm. Those without axillary metastases totaled 21 (21 per cent) and of these, 15 (71.4 per cent) developed edema of the arm.

The circumferences of the mid-upper and mid-lower arm were measured before the start of therapy and at return visits following completion of the treatment described above. Adapting Daland's classification to this series, we have di-

vided the cases into four groups: group 1, no swelling (0 to 0.5 cm.); group 2, slight swelling (1 to 2 cm.); group 3, moderate swelling (2.5 to 4.5 cm.); and group 4, severe swelling (5 cm. or more).

Measurements of Homolateral Arm Following Radical Mastectomy and Postoperative Irradiation

In group 1, there were 37 patients (37 per cent) who had no swelling in the upper arm, and in 39 patients (39 per cent) there was no swelling in the lower arm (table 1). Daland found that 45 per cent of the upper arms and 55 per cent of the lower arms, in his series of cases, had no swelling.

In group 2, 25 patients (25 per cent) were found to fall into this category. Six had an increase of 1.0 cm., 12 an increase of 1.5 cm., and 7 an in-

TABLE 1
Measurements of homolateral arm following radical mastectomy and postoperative irradiation (Georgetown University Medical Center Series)

	Upper Arm		Lower Arm	
	no.	%	no.	%
No swelling				
Decrease	10	37	15	39
No change	21		16	
Increase 0.5 cm.	6		8	
Slight swelling				
1 cm.	6	25	10	29
1.5 cm.	12		12	
2 cm.	7		7	
Moderate swelling				
2.5 cm.	11	19	8	21
3 cm.	2		3	
3.5 cm.	1		2	
4 cm.	1		5	
4.5 cm.	4		3	
Severe swelling				
5 cm.	7	19	1	11
5.5 cm.	3		3	
6 cm.	1		0	
6.5 cm.	2		0	
7 cm.	1		2	
7.5 cm.	2		1	
8 cm.	1		1	
9 cm.	1		2	
10 cm.	0		1	
11 cm.	1		0	
Total	100		100	

crease of 2.0 cm. Of the lower arm measurements, 29 patients (29 per cent) had this "slight" swelling. Daland found 31.0 per cent of his patients to have "slight" (group 2) swelling in the upper arm and 27 per cent in the lower arm.

In our group 3, 19 patients (19 per cent) were so classified with swelling in the upper arm. In 15 of these individuals, the range was 2.5 to 4.0 cm., and 4 had an increase of 4.5 cm. In 21 patients (21 per cent) there was swelling in the lower arm of 2.5 to 4.5 cm. Daland's series, in comparison, revealed 17.0 per cent with moderate (group 3) swelling in the upper arm and 10 per cent in the lower arm.

In group 4, 19 patients (19 per cent) had involvement in the upper arm. The increase in circumference was 5.0 cm. in 7 patients, 5.5 cm. in 3, and 6.0 to 9.0 cm. in the remaining 9 individuals. In regard to the lower arm, 11 patients (11 per cent) had severe swelling. Daland reported an incidence of but 5.5 per cent severe swelling in the upper arm, and 6.6 per cent in the lower arm. Of possible significance is the fact that 4 of Daland's 5 cases with severe swelling of the upper arm and 2 of his 6 cases of severe swelling of the lower arm received x-ray therapy.

To reiterate, we have divided our cases in a similar fashion to those recorded in Daland's report. We have, however, arbitrarily selected the figure of a 2-cm. increase in circumference (group 2) as the figure at which, or below which, the swelling appears not to be clinically significant. This is listed as Daland's "slight swelling" group. Thus, only those with moderate or severe swelling have significant lymphedema. Utilizing this standard we find 38 per cent (38 cases) of the upper arms and 32 per cent (32 cases) of the lower arms in this series to have significant swelling. Again referring to Daland's figures, we find his moderate and severe groups total 22.5 per cent and 16.6 per cent for the upper and lower arms, respectively. Thus it appears, in comparing a series in which few cases received postoperative x-ray therapy to one in which all cases were so treated, that postoperative irradiation does increase the likelihood of postmastectomy lymphedema in patients so treated (table 2).

We have seen lymphedema regress spontaneously in a few cases, but not completely in all of these. This has usually occurred over a period of several months. Over a 4-year period, in 1 case, there was a gradual regression of 3.0 cm. in the

TABLE 2
*Comparison of homolateral arm measurements in Georgetown University Medical Center Series with those reported by Daland**

	Georgetown Series† X-ray therapy				Daland Series‡			
	Upper arm		Lower arm		Upper arm		Lower arm	
	no.	%	no.	%	no.	%	no.	%
No swelling.....	37	37	39	39	41	45	50	55
Slight swelling...	25	25	29	29	28	31	25	27
Moderate swelling.....	19	19	21	21	16	17	9	10
Severe swelling.	19	19	11	11	5	5.5	6	6.6
Significant swelling.....		38		32		22.5		16.6

* Daland, E. M., modified from table in New England J. Med., 242: 497, 1950.

† All cases in this series received postoperative x-ray therapy.

‡ Few cases in this series received postoperative x-ray therapy.

circumference of the arm; at the end of 6 years, there was no additional change. Of 31 cases, followed from 3 to 9 years and having significant edema, 8 cases (25 per cent) showed a gradual, spontaneous regression of 2 cm. or more. We, therefore, cannot agree entirely with the statement that, once established, the process of postoperative lymphedema of the arm is irreversible. Measures such as sleeping with the arm elevated on pillows and elevating the arm for periods during the day, may limit the process and may even effect a change for the better. In severe cases, it may be necessary to wear an elastic bandage on the arm to limit the swelling. In none of our cases has severe pain and/or disability been encountered. We have observed, however, that in those individuals with marked postoperative drainage, wound infection and poorly placed incisional scars, the edema tended to be more severe. Exact figures are not available to us in this series because there are a few patients on whom we are not able to get complete data as to the postoperative course, including the presence or absence of infection, the use of drains and many other details.

Operative procedures for the correction of lymphedema are reported sporadically^{14, 17, 26, 33} and with encouraging results in isolated cases. As

we have noted, however, every effort should be made at operation and in the immediate postoperative period to avoid factors leading to lymphedema which are preventable. We have had no experience with the development of lymphangiosarcoma in edema of the arm, as has been reported in the literature.^{7, 19, 20, 27}

SUMMARY AND CONCLUSIONS

An analysis of 100 cases of carcinoma of the breast treated by radical mastectomy and postoperative x-ray therapy, in which careful measurements of the circumference of the arms were made at intervals following therapy, is presented.

Arbitrarily selecting a 2.0-cm. increase in circumference as a standard at or below which we think edema is not significant, we found significant edema in 38 per cent of the upper arms and 32 per cent of the lower arms measured.

In comparison with Daland's series, in which but a few cases received irradiation therapy, our patients showed an increased incidence of lymphedema of the arm, following postoperative irradiation about the axilla.

Postmastectomy lymphedema of the arm is not necessarily an irreversible process. In 25 per cent of our cases, followed from three to nine years, showing significant edema of the arm (above 2.0 cm. in circumference), a gradual, spontaneous regression was noted, although in some cases residual edema was present.

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SPONTANEOUS HEMOPNEUMOTHORAX

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INTRODUCTION

Spontaneous hemopneumothorax, although a relatively rare condition is one of real interest which has occupied the attention of writers for centuries. Laennec¹³ is credited with the earliest recognition of this condition, however, his writings as well as those of Littré¹³ are not concise as to its exact nature and it is possible that confusion existed in their minds. In 1900 Pitt²⁰ reported a case which ended fatally. He named the condition and postulated rupture of an emphysematous bulla as the cause. In the same year Boland² and Rolleston²⁴ reported a case each. These men are credited with the first accurate description of this condition and established it as a clinical entity by giving the name spontaneous hemopneumothorax.¹⁰ Our interest in the subject has been aroused by a larger number of cases than are reported herein, however, those which are reported seem to illustrate some point or facet of the problem and these are reported in some detail.

THE PROBLEM IN GENERAL

Although spontaneous pneumothorax is by no means an uncommon condition, its complication by spontaneous intrapleural hemorrhage is uncommon. Fry and associates¹⁰ collected 174 cases reported up until 1954, and added 13 cases of their own. It is generally accepted that the majority of cases of idiopathic spontaneous pneumothorax are due to rupture of a subpleural cyst or bulla. The accumulation of air within the pleural space induces collapse of the lung and even tension pneumothorax may be produced. If pre-existing adhesions between the visceral and parietal pleurae are put on stretch they may rupture or tear and the free ends of such torn adhesions have been observed by us to continue to bleed over a long period of time (case 5).

Usually when a relatively small vessel carries blood under arterial pressure, it is an artery whose wall consists of tunica intima (endothelium), tunica media (muscle fibers, unstriated in type, bound together in more or less spiral strata), and

tunica externa (mainly fibrous tissue containing many fibrous tissue cells).²³ Contrast the ability of a vessel so formed to aid in the process of clotting by retraction and narrowing or closure of its bleeding end, with that of the vessels contained in these pleural adhesions. In this latter case the vessels are of poor quality in so far as they are able to function as arteries because they are scarcely more than endothelial lined fibrous tubes (fig. 5). Nevertheless, they are called on to carry blood under systemic arterial pressure and when the adhesion containing such a vessel is torn, that vessel is incapable of retraction or contraction, and this valuable aid to clotting and the arrest of hemorrhage is absent. Thus it is that profuse and prolonged bleeding occurs from the ends of these torn adhesions.

The position of the torn adhesion, high in the apex of the thorax or high in the mediastinum or even on the apex of the upper lobe, allows the bleeding to continue uninfluenced by juxtaposed lung or other tissue or even by clot itself.

Thus the bleeding is uninhibited by the usual factors that aid clotting and the amount of hemorrhage is usually excessive and may continue to the point of exsanguination and death.

Often it is difficult to determine the onset of intrapleural bleeding in spontaneous pneumothorax. The presence of a fluid level seen within the pleural space on chest x-ray should place one on guard even in the absence of shock. It is wise to rely on "upright films" if the patient's condition permits such an x-ray examination. Diagnostic thoracentesis easily and conclusively establishes the diagnosis. Close observation of all patients with spontaneous pneumothorax is therefore indicated and transfusions and thoracentesis should be employed whenever hemorrhagic shock exists. If bleeding is rapid and uncontrolled, open thoracotomy is indicated. In "any patient with spontaneous pneumothorax who is in collapse when first seen or who suddenly goes into that state, massive intrapleural hemorrhage must be considered."

The symptoms may simulate those of per-

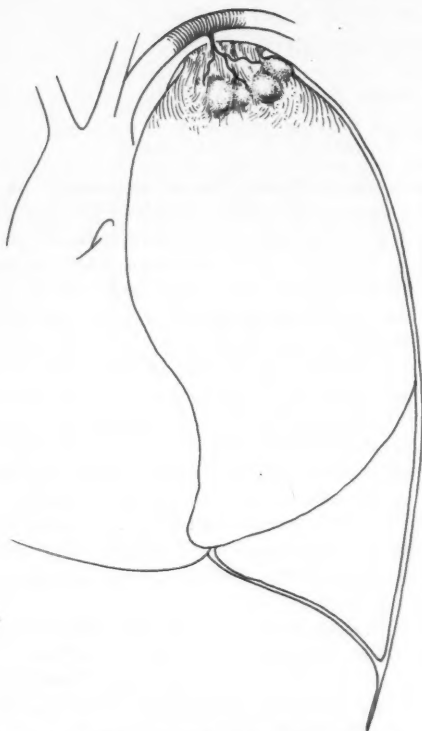


FIG. 1. Diagram to show the presence of apical subpleural blebs and apical pleural adhesions.

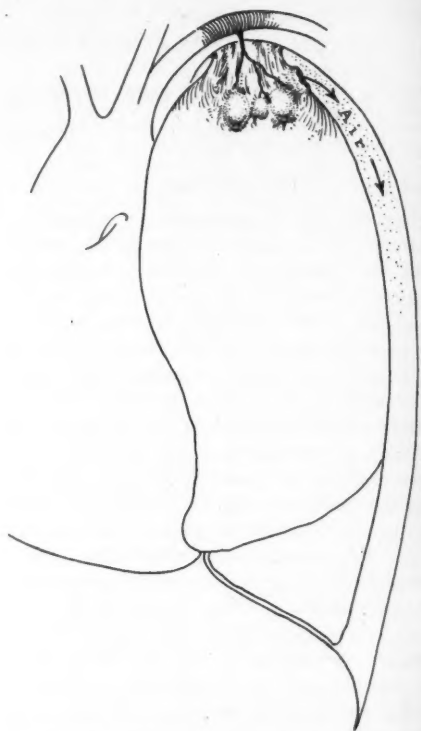


FIG. 2. Illustrates rupture of subpleural bleb with escape of air into the pleural space, thereby causing spontaneous pneumothorax.

forated gastric ulcer or acute myocardial infarction. Occasionally a case may be in danger of exploratory laparotomy because some intraperitoneal catastrophe is suspected. More than once a patient has been spared laparotomy because an upright film of the upper abdomen (and lower chest) has been made in an effort to discover subdiaphragmatic free air from a perforated viscus; the film has shown hydropneumothorax instead.

The sex and age incidence of spontaneous hemopneumothorax is often stated thus: "It is a disease of young males." Only 7 cases have been reported in females^{8-10, 12, 13, 15, 28} (one case is added herewith, case 5), and although reported cases range in age from infancy to old age, by far the majority of cases occurs in men between 20 and 40 years of age with an average of 28 years.¹⁰

Reported cases indicate that there is no predelection for either side of the thorax; incidence in reported cases is almost equally divided between right and left.

Although 3 cases have been reported in Negroes and 1 in a Chinese, the reported cases are almost exclusively white patients.¹⁰

ETIOLOGY

Twenty years ago, tuberculosis was thought to be the basic cause of spontaneous pneumothorax; however, the past decade has seen the emergence of spontaneous rupture of subpleural blebs or bullae as the most likely cause. Since the development of pneumothorax precedes the development of hemothorax in these cases the relation of the latter to the former is obvious and indeed in some cases no other cause for bleeding can be found than the ruptured blebs (and their vessels) themselves (case 1).^{7, 11, 17} There is no general agreement regarding the cause of these bullae or their exact pathogenesis, but all writers give rupture of these cysts, bullae or vesicles as the cause of spontaneous pneumothorax.

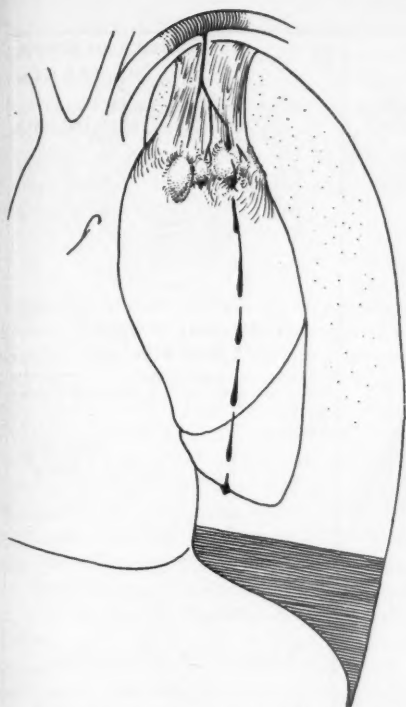


FIG. 3. The pneumothorax increases; the apical pleural adhesion is put on stretch and bleeding begins.

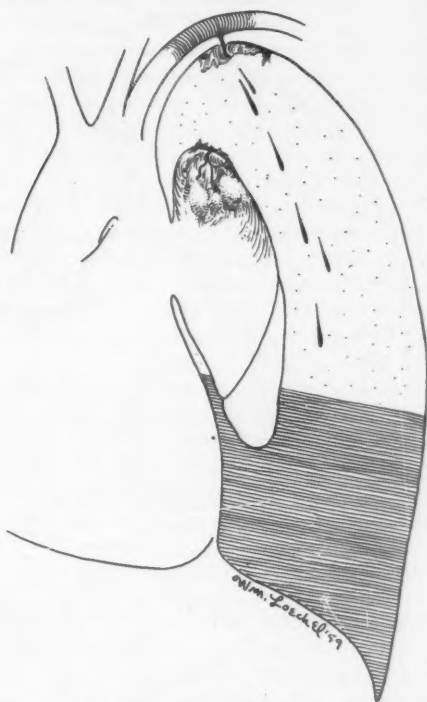


FIG. 4. Pulmonary collapse is far advanced. The adhesion tears allowing profuse and continuing bleeding.

Intrapleural bleeding in large amount is thought to come from the chest wall or mediastinum, and as previously stated, to occur from parietal ends of torn pleural adhesions. In one of our cases (case 5), the bleeding was coming from a single large vascular adhesion which was situated high in the apex of the chest near the subclavian artery. At the time of thoracotomy, this vessel spurted constantly with great force and without any evidence of an attempt at spontaneous clotting or retraction. In other cases the rate of bleeding was not so spectacular and was either an ooze or occurred in drops. The foregoing seems to be the usual occurrence; however, massive bleeding may occur from large pulmonary vascular channels ruptured at the time of rupture of the cyst (case 1).

The relationship of physical exertion as a cause of the rupture of these cysts or bullae is open to serious question. Certainly in our series of cases none occurred during violent exertion or exercise and in ours, as well as most of the series reported,

the onset of the spontaneous lung collapse characteristically occurred while the patient was at rest. It has been postulated that exertion may cause increase in tension within the bleb which subsequently ruptures as a result of prolonged ischemia of its wall, and is in turn followed by collapse of the lung with tearing of the vascular adhesions and hemorrhage.

In compensation cases, the relationship of exertion during the time on the job to the occurrence of these conditions is important and as yet unanswered. Indeed, if exertion is not the cause of bleb rupture once the rupture has occurred, it seems logical that strenuous physical labor may aggravate the condition and thereby bring it into a compensable category. Undoubtedly exertion will adversely affect intrapleural bleeding. In one case reported herewith (case 1) it seems likely that violent exercise associated with vomiting and retching may have so aggravated the condition that death occurred.

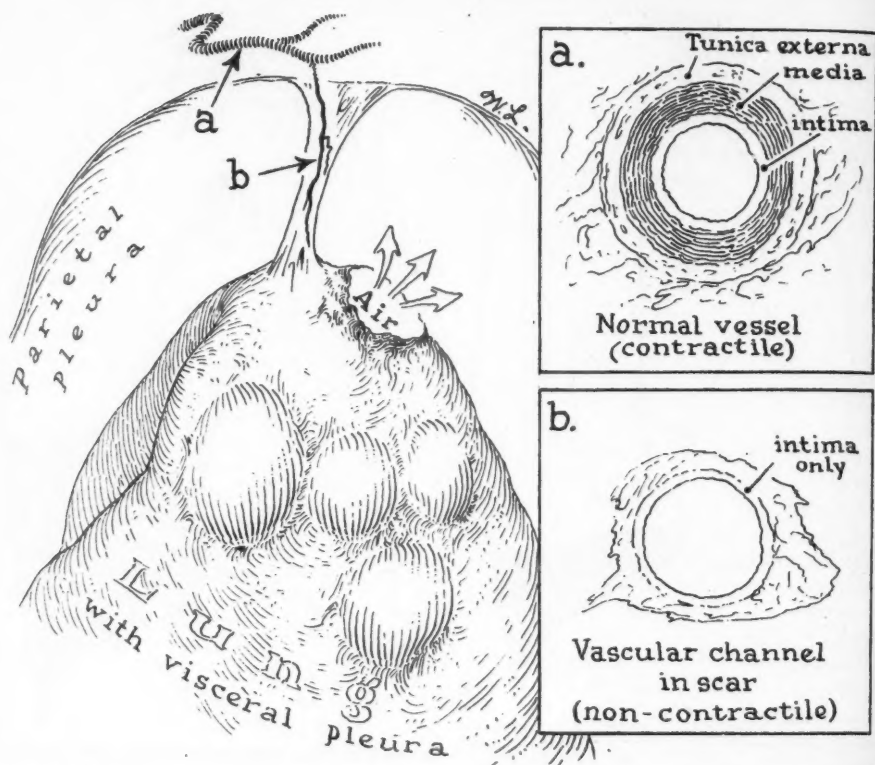


FIG. 5. Detailed semi-diagram illustrating the blebs (one of which has ruptured), pneumothorax and the apical adhesion put on stretch. Also, the inserts (a and b) contrast the difference between a normal artery and the vessels contained in the adhesion.

THE CLINICAL PICTURE

Pain is usually present at the onset of spontaneous hemopneumothorax and although the pain is usually mild or moderate it may be very severe. Characteristically, the patient experiences a mild but sudden pain in the affected side of the chest and later a more severe pain supervenes which becomes progressively worse. Shortness of breath, "tightness in the chest," "belching," a "feeling of being too full" develop, and marked dyspnea, sweating, pallor, weakness and shock may follow. The patient is apprehensive and usually wishes to be in bed, but in a sitting position. Cyanosis may be present.

At times the symptoms may simulate coronary occlusion whereas at others, the patient may be thought to have an abdominal surgical emergency. The pain may be so intense and radiate to

the abdomen to such an extent that the patient may be in danger of exploratory laparotomy.¹⁶

It may be difficult to determine the onset of hemorrhage in cases of spontaneous pneumothorax when the clinical symptoms and signs of hemorrhagic shock are absent. In such cases, diagnostic thoracentesis will settle the question whenever fluid is present in conjunction with air in the pleural space.

Thus, physical signs, chest x-ray, diagnostic thoracentesis, in addition to hematocrit and red cell counts and hemoglobin determination must all be employed in diagnosis. Electrocardiography, upright films of the abdomen to rule out perforated viscus, as well as determination of blood enzyme activity may be required to clarify the situation and rule out coronary occlusion and acute pancreatitis.

Usually the condition presents a straightforward picture of onset with pain and tightness in the chest followed by difficult breathing, aggravation of pain and the onset of weakness and shock. Chest x-ray or fluoroscopy will show the collapsed lung, even with marked mediastinal shift and tension pneumothorax in some cases, and give evidence of fluid in the chest.

TREATMENT

Depending upon the seriousness of the patient's condition, vigorous and emergency measures may be required to save life. Relief of tension pneumothorax by thoracentesis and treatment of hemorrhagic shock by whole blood transfusion may be lifesaving. Conversely, if the seriousness of the patient's difficulty is not appreciated and he is allowed to remain in shock for a period of hours, particularly if large doses of morphine are employed, fatal outcome may ensue (case 1). It should be emphasized that any patient suffering from spontaneous pneumothorax should be handled with caution and should not be heavily sedated to "carry him over" until a convenient time for thoracentesis, or a time when thorough consideration of his case is possible. Such expectant handling may result in death. The use of a Clagett cannula attached to a water-sealed bottle may be lifesaving, particularly in cases of tension pneumothorax. Blood transfusion, oxygen inhalation and other general supportive measures must be employed and are of extreme importance.

Treatment must have as its immediate goal, functional re-expansion of the collapsed lung and the restoration of circulating blood volume. Prevention of further hemorrhage by ligation of the bleeding source and prevention of recurrence of spontaneous pneumothorax in the future are also therapeutic aims. The methods of accomplishing these aims and the time of their employment have been the source of much contradictory advice in the literature. Delay in evacuation of intrapleural blood to "compress the bleeding source," to "favor clotting" and thereby prevent further hemorrhage is to be condemned and may result in death, or a patient too moribund to withstand thoracotomy. Repeated aspirations may help prevent fibrothorax but if bleeding persists and thoracentesis yields an amount of blood approaching a liter, thoracotomy is indicated. An increasing pulse rate in such a patient with hemopneumo-

thorax, being treated by thoracentesis, is a valuable guide to an early thoracotomy.⁵

Treatment must also eliminate fibrothorax and its inherent bad effects on pulmonary function, as well as its possibility of fostering pleural sepsis. As indicated above, repeated thoracentesis will aid in accomplishing this aim. The use of fibrinolytic enzymes is widely advocated^{18, 21, 26} but in our hands has yielded disappointing results. Indeed, without exception, the instillation of streptokinase and of streptodornase into the affected pleural space have caused the patient to become quite ill. The patients have chills, severe chest pains, and the temperature may rise to 106°, and in some cases intrapleural bleeding may be restarted or be increased by the use of these enzymes (case 2). Finally, we have failed to find a case in which the employment of these enzymes changed the intrapleural situation enough to prevent the necessity for thoracotomy on this basis alone. Our experience with intrapleural trypsin has been similar.

Thoracoscopy, once in vogue and advocated by some^{1, 6, 12} seems to have little or no place in the treatment of spontaneous hemopneumothorax today. Thoracostomy^{3, 4, 14} using tube drainage has been employed and we have in some cases used Clagett cannula drainage. Fry and associates¹⁰ caution that if thoracostomy is employed, a simple underwater seal should be used, further stating that if early suction drainage is employed, severe bleeding may result.

If the situation has developed in such manner that primary thoracotomy has been avoided and even if the measures above have been employed, decortication may still be necessary to overcome residual fibrothorax. In late cases, the lung may fail to expand, and owing to the rapid defibrination of blood in the pleural space, the lung may be bound by a fibrinous envelope. Thoracotomy and decortication will afford an opportunity to remove the "peel" from the visceral pleura, and when chest wall function is stopped and/or the diaphragm made immobile, these areas likewise can be decorticated. Although ideal results are not always obtained, improvement in pulmonary function usually ensues.^{19, 25, 27, 28} Resection of the bleb-bearing area is usually possible and should be done at the time of thoracotomy. Bronchopleural fistula may be present, but is rarely troublesome in spontaneous hemopneumothorax, and resection

of the area of air leakage usually obviates this difficulty.

Procedures designed to prevent recurrent pneumothorax, other than segmental resection of the bleb bearing area, are seldom necessary. Poudrage, and intrapleural instillation of silver nitrate have been used but probably aren't necessary. The causing of sterile pleuritis by any means seems unnecessary because the intrapleural blood itself seems to be adequate stimulus for the formation of adhesive pleuritis, once complete reexpansion of the lung is accomplished. Nevertheless, our practice is to rub the visceral and parietal pleurae with gauze to cause sterile pleuritis in order to favor a symphysis.

Thus, the therapeutic problem is solved by overcoming the deleterious effects of pneumothorax by aspiration of air from the pleural space, either intermittently or continually and by overcoming the deleterious effects of massive hemorrhage by supportive measures and blood replacement, but of highest priority is ligation of the source of bleeding if it fails to clot spontaneously. Thoracotomy is mandatory in some cases, and certainly advisable in most.

PROGNOSIS AND MORTALITY

The reported mortality in spontaneous hemopneumothorax is 12 per cent.¹⁰ In our series, 1 fatal case is recorded. The morbidity incident to this condition and the loss of time from work is great. In some instances the cases requiring thoracotomy, when properly handled, are restored to useful life more quickly than those treated by multiple aspiration or continuous drainage. Fry and associates¹⁰ state that two months' time is required, on the average, for complete reexpansion of the lung following the removal of blood from the pleural space. Some cases will come to decortication despite diligent aspiration efforts even in an early recognized case.

On the other hand, if the true situation is promptly recognized and proper procedures instituted, mortality is low and prognosis excellent with reduced morbidity. In the face of such little risk involved in thoracotomy, as performed today, and since the proper application of therapeutic principles is most easily afforded by this procedure, we strongly advocate early thoracotomy in such cases of severe progressive hemopneumothorax. In our hands, this method of treatment has resulted in no fatality, has reduced morbidity

far below that reported for "conservative" management and thereby made prognosis excellent. There has been no recurrence of pneumothorax in our series, although such has been reported.^{10, 22} No case of recurrent spontaneous hemopneumothorax has been reported, to our knowledge.

CASE REPORTS

*Case 1.** G. G. T., a 35-year-old white man, was admitted to the Suburban Hospital at 7:00 p.m., September 7, 1955, with a diagnosis of spontaneous pneumothorax. He had been perfectly well and had no serious illness until the morning of September 6, when he noted pain in the left chest. He went to work; however, the pain persisted and he saw a physician, at his place of occupation, who noted nothing serious and the patient was told that he had probably "pulled a muscle." The following morning the pain was more severe and he was unable to move or breathe without pain. He was seen at noon by his physician who suspected that he had a pneumothorax on the left side. At this time he was not unduly dyspneic, nor did he appear to be dangerously ill and he was sent to the office for a chest x-ray. The films were reviewed at 4:00 p.m. and they confirmed the impression of spontaneous pneumothorax. There was 80 per cent collapse of the left lung and a small amount of fluid in the base of the left pleural cavity. He was sent into the hospital for a chest tap, to be done the following morning. There was no history of injury. When seen in the hospital he was a lemon-yellow color, had very shallow rapid breathing and was in obvious pain. His blood pressure was recorded at 98/60 but the heart sounds were of good quality.

A review of the nurse's notes indicates that on admission the patient was extremely ill. He was very uncomfortable and because of his constant complaint, a grain of codeine was administered hypodermically at 8:15 p.m. Following this, he vomited suddenly, his pulse was weak and rapid and his blood pressure was 96/66. He perspired profusely, he moaned and his eyes rolled back in his head. The resident was called and again a grain of codeine was administered. He continued, however, to be very uncomfortable and to vomit occasionally, and between 10:25 p.m. and 3:45 a.m., he was seen at frequent intervals by the resident-on-call and various sedative medications were administered. At 3:45 a.m., $\frac{1}{4}$ of a grain of morphine was administered and following this, the patient complained of pain only when his position was changed. He appeared to be sleeping from 5:00 to

* This case was not seen by us while the patient was alive, and is reported through the courtesy of Dr. John J. Curry, Wheaton, Maryland.

5:30 but from 5:30 a.m. onward, he was in constant distress which increased in severity and he did not respond to an additional grain of codeine, which was given at 5:40. At 7:30 a.m., his condition was noted as very poor and the night nurse's report was "quite unsatisfactory." At 8:00 a.m., he was very restless and apprehensive and complained of shortness of breath. Nasal oxygen was started; however, the patient continued on his downhill course and expired suddenly at 8:55 a.m.

Permission for postmortem examination was granted and the abdomen was opened first. It was noted that the left diaphragm bulged some three fingers' breadth below the left costal margin and when a needle was inserted through this diaphragm into the chest, air escaped as though under pressure. In addition, thoracenteses in intercostal spaces on the left, likewise, showed evidence of tension within the pleural space. When the chest was opened, about 4000 cc. of frothy red blood and fibrinous clots were present. The left lung was completely collapsed against the mediastinum. Unfortunately, there is no note made relative to the presence or to the absence of parietal pleural adhesions. The surface of the left lung was wrinkled and of dark purple color, and there were still remnants of small emphysematous blebs visible in the apex. On careful inspection of the apex, there was revealed a small area covered with red fibrin. On removing this fibrin, there appeared to be a small tear due to rupture of a small bleb. Several blood vessels in this area were found to be open and were quite evident in the exposed parenchyma. On section, the parenchyma appeared to be congested and showed a small area of hemorrhage. No other abnormality of interest was noted.

Comment. This case represents one of fatal termination from spontaneous hemopneumothorax in a young, previously healthy and vigorous white man. It illustrates the necessity of prompt attention to persons suffering from hemopneumothorax and particularly emphasizes the dangers in expectant treatment. No doubt the situation was aggravated by the strenuous activity incident to violent vomiting.

Case 2. L. M. H., a 33-year-old white man, was admitted to Mt. Alto Veterans Hospital, on July 10, 1951, complaining of particularly severe pain in his left chest. He stated that 24 hours before admission, while sitting at rest, he noticed sudden onset of sharp pain in his left chest which radiated into his left arm and shoulder and neck. He became short of breath and experienced dizziness. He did not faint. He sought admission to the hospital and a chest x-ray showed partial pneumo-

thorax and a small pleural effusion on the left side. At the time of his admission to the medical service, his temperature was 99.4°, his pulse was 88 and his blood pressure was 128/94. His chest film now showed a fluid level up to the 8th rib posteriorly and displacement of the mediastinum to the right with complete collapse of his left lung. His white blood count on admission was 28,800 with a shift to the left; red blood cells were reported as 3,100,000 and a hematocrit of 34 per cent. Bleeding time was 45 seconds and coagulation time, 8 minutes; platelets, 260,000 per mm.³ of blood. Electrocardiogram showed inverted T-waves in lead one but otherwise showed no significant abnormality.

On the 1st day of his admission to the hospital, a thoracentesis was done on the left and 500 cc. of blood were removed along with a considerable quantity of air. Following this, an x-ray was done which showed an increase in the amount of collapse of the lung and a higher level of fluid in the left pleural cavity. The 2nd day, 1400 cc. of bloody fluid were removed from the left chest and 1000 cc. of blood were given by transfusion. On the 3rd day, left thoracentesis produced 1900 cc. of bloody fluid and on this day the patient received 1500 cc. of blood transfusion. His blood pressure was 140/80 and was stable. His pulse was 90 to 120. On the 4th day, thoracentesis produced 800 cc. of blood. On the 5th day, thoracentesis produced 250 cc. of blood and by this time the hematocrit on the blood removed at thoracentesis had dropped to 5 per cent. On the 7th day, thoracentesis produced 25 cc. of bloody fluid and on this date 100,000 units of streptokinase and 25,000 units of streptodornase were injected into the pleural space. The patient experienced severe pain and high fever following this injection and was uncomfortable the entire night. He complained of severe pain in his epigastrium, dyspnea and his blood pressure fell to 100/60. X-ray of the chest following this injection showed a reaccumulation of fluid in the left chest and when thoracentesis was done, a very bloody effusion was removed which looked almost like pure blood and in the amount of 800 cc. On this day he was given an additional 500 cc. of blood in transfusion. On the 8th day, 1000 cc. of blood were given by transfusion and thoracentesis produced 500 cc. of blood. On the 9th day, July 18, 1951, surgical consultation was sought and thoracotomy was recommended. This was accomplished in addition to bronchoscopy, without incident. Bullous lesions in the left apex were resected and a decortication of the lung was accomplished. The site of bleeding was not entirely clear but one of the operators (F. S. A.) had the impression that the bleeding site was in the parietal pleura about the level of the third interspace in the midaxillary

line. This was difficult to ascertain, however, for the entire parietal and visceral pleura was covered with a thick coating of fibrin. The patient recovered uneventfully.

Comment. This case represents spontaneous hemopneumothorax resulting in massive intrathoracic bleeding of such alarming proportion that exploratory thoracotomy was necessitated. It also illustrates the difficulties of using fibrinolytic enzyme intrapleurally in such cases. Not only did this patient experience severe discomfort following its use but it seems that the bleeding, which had become minimal, was again started and this actually precipitated the necessity for thoracotomy. It would also appear that prolonged bleeding necessitating rather massive total transfusions might have been avoided by early thoracotomy. (Total blood removed by thoracentesis was 5000 cc. Total transfusion before exploration was 4000 cc.) The patient made good recovery following decortication and at the time of discharge his vital capacity was 90 per cent of normal.

Case 3. W. K., a 25-year-old white man, was admitted to Providence Hospital, complaining of severe pain in the left chest and extreme shortness of breath. The onset was while the patient was at rest. He was employed in a dry cleaning establishment and had inhaled irritating fumes from solvents but denied any previous respiratory difficulties.

On admission, his temperature was 99.6°, his pulse 120, and his respirations, 24 per minute. He was pale, weak and perspired profusely. Physical examination was consistent with left pneumothorax. His blood pressure was 90/60.

An upright x-ray of his chest showed the left lung collapsed against the mediastinum and a fluid level extended up to the 6th rib posteriorly. A thoracentesis confirmed the presence of blood as well as air in the left pleural space.

A 1000-cc. whole blood transfusion was administered and a Clagett cannula was inserted into the left thorax and attached to a water-sealed bottle.

These measures resulted in gratifying improvement in the patient's condition and allowed thoracotomy to be done about 2 hours after his admission.

A left thoracotomy was done and some 2000 cc. of liquid blood were found in the pleural space. The source of bleeding was a long adhesion high in the apex of the left thorax which spurted blood freely but was easily controlled by suture ligature. The apex of the upper lobe contained many blebs and scars and a leak of air could be demonstrated in this area.

Segmental resection of the bleb bearing area was accomplished. The surface of the lung and the parietal pleural surfaces were rubbed with gauze and the lung expanded well.

The patient recovered without incident, left the hospital on the 10th postoperative day and has remained well since.

Comment. This is an almost classical case of spontaneous hemopneumothorax and represents, we feel, the good result obtainable by prompt thoracotomy.

Case 4. C. P., a 22-year-old white man, was admitted to Suburban Hospital on March 16, 1958, with sudden onset of sharp right-sided chest pain. The patient had no history suggesting an episode of spontaneous pneumothorax. Following admission, chest film revealed 30 per cent collapse of the right lung, and a fluid level low in the chest. He remained at bed rest for 6 days, with no change in his condition except for a minimal amount of re-expansion of the right lung. He was seen by us March 22, 1958. Thoracentesis brought out 650 cc. of unclotted blood posterolaterally, and an anterior Clagett needle, with closed drainage system, delivered the air. The following day, the lung was fully expanded except for a very small amount of fluid at the costophrenic angle. The air leak closed spontaneously, and the lung remained expanded following removal of the Clagett needle. He has continued to remain well.

Comment. This case illustrates the value of prompt institution of therapy. In this instance the bleeding was not so excessive as in the previous cases and a good result was obtained by more conservative therapy.

Case 5. K. S. O., a 37-year-old white woman, was admitted to the U. S. Naval Hospital on October 24, 1951, complaining of severe pain in the right chest of 10 hours' duration. An admission diagnosis of lobar pneumonia was made and therapy and diagnostic procedures consistent with this diagnosis were instituted. During the first day in the hospital, however, her chest pain became much more severe and the patient developed marked difficulty in breathing. Chest x-ray on the evening of admission revealed a right hemopneumothorax, with evidence of about one-third collapse of the right lung. The following morning the patient was in mild shock with a blood pressure well below 100 mm. Hg systolic and it was thought advisable to start a transfusion. Whole blood, 500 cc., was administered intravenously and at that time 500 cc. of blood was withdrawn from the right thorax by thoracentesis. On October 25,

1951, the patient continued to go into shock on two more occasions and additional transfusions were given. Her progress continued to be downhill and finally on October 26, 1951, a surgical consultation was requested and immediate thoracotomy was advised. This was accomplished without incident and a large amount of blood, estimated to be 4000 cc., was evacuated from the chest and a freely bleeding apical adhesion was found and ligated; following this, no further hemorrhage occurred. The area of blebs in the apex was resected and the lung closed with interrupted stitches. The parietal pleural surface as well as the visceral pleural surface was rubbed with gauze and the lung was expanded. There was no evidence of leakage at the close of the procedure. The patient withstood this procedure well and returned to her room in good condition. She received 2000 cc. of whole blood by transfusion before the operation and during surgery received an additional 1000 cc. of blood. Postoperatively, she did very well, made an uneventful recovery and left the hospital November 5, 1951. She has had no recurrence of difficulty.

Comment. This case is interesting because it is a case of spontaneous hemopneumothorax occurring in a young white woman. It illustrates well how serious the bleeding can be in an unrecognized case and also shows the usual gratifying response to proper therapy.

Case 6. H. C., a 19-year-old white man, was in his usual state of good health until the evening of July 22, 1958, when he suffered the sudden onset of pain in the right chest. This soon extended to the right shoulder. Breathing became difficult. A physician was not summoned until the following morning. At this time, he was admitted to Suburban Hospital with a diagnosis of right spontaneous pneumothorax. He was not in severe distress and complications were not anticipated; however, by 1:00 p.m. his condition had worsened considerably. When seen, he was pale, dyspneic, with pulse 150 per minute and blood pressure 70/50. Films that morning had been made supine, and had not caused concern because a fluid level was not seen, and no estimate was made of the amount of fluid in the chest. Repeat upright portable films showed an almost complete collapse of the lung, a large amount of fluid and a level at the height of the 6th posterior rib. Thoracentesis via a Clagett needle yielded 1800 cc. of liquid thick blood, plus an unmeasured, but large, amount of air. Rapid blood replacement was started as soon as possible, and the patient rallied. When out of shock, he was taken to the operating room, and a thoracotomy was done. An additional

1200 cc. of clot and liquid blood were evacuated. The bleeding site was a torn adhesion at the very apex of the right lung, producing a tangential wound in the wall of a subpleural vein. Suture ligation of the bleeding point was performed, plus wedge resection of fibrosis and emphysema at the lung apex. The pleural cavity was lavaged, and closed drainage instituted. Blood replacement totalled 3000 cc. He had an uneventful postoperative recovery.

There had been no previous episode of spontaneous pneumothorax.

SUMMARY

Spontaneous hemopneumothorax has been recognized since the time of Laennec but was first so named and explained in 1900. It is a disease, characteristically, of young white men. It may occur in women. A classical case occurring in a 37-year-old woman is reported.

The origin of the air leak seems to be rupture of a subpleural bleb. Factors influencing this occurrence are not clear. Certainly a relation to violent activity doesn't seem to exist. The severe hemorrhage complicating the pneumothorax may arise from various sources but characteristically, a pre-existing pleural adhesion is torn as the lung collapses. The blood vessels in this adhesion are abnormal in that their walls contain no contractile elements but the vessel carries systemic blood pressure. Continued bleeding occurs because the normal aids to clotting are not brought into action (vessel contraction and retraction; juxtaposed viscera or clots).

Bleeding may be massive and the condition may be fatal in a relatively short time. Such a case is reported. If not fatal, the morbidity induced in these cases is great due to the formation of fibrothorax and its deleterious effect on pulmonary function.

Mortality and morbidity may be eliminated or greatly reduced by proper treatment. This is discussed. It is to be emphasized that primary thoracotomy prevents mortality and may greatly reduce morbidity. Decortication may reduce the morbidity from late complications of hemopneumothorax.

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NONPARASITIC HEPATOCYSTIC DISEASE: A REPORT OF NINE CASES

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The earliest reported case of nonparasitic cystic disease of the liver was that by Bristowe in 1856.² This author first pointed out the association of this lesion with polycystic renal disease. In the succeeding century approximately 500 additional cases of nonparasitic liver cysts were reported. Periodically, as interest revived, exhaustive reviews of the literature have been undertaken. Boyd¹ in 1913 collected 34 cases; Jones¹² in 1929 reported 60 cases; 104 cases were reported by Stoesser and Wangenstein¹⁸ in 1929; and Davis³ in 1937 collected data on 499 cases, of which 226 were diagnosed at surgery and 273 found at post-mortem examination. Of these 187 were single unilocular cysts, 20 were solitary but multilocular, 241 cases had multiple cysts, and 51 were not classified.

The most recent comprehensive review is that of Henson and associates.⁷⁻⁹ This work also reviews all cases seen at the Mayo Clinic from 1907 to 1954. These consisted of 38 cases of single unilocular cysts, 29 cases of multiple cysts and 5 cases of traumatic or pseudocysts.

Nonparasitic cysts of the liver may be single or multiple, either of which may be unilocular or multilocular. The following classification of hepatic cysts proposed by Jones,¹² based on histogenesis, is commonly accepted.

A. Parasitic

1. Echinococcal (hydatid)

B. Nonparasitic

1. Solitary (simple retention)
2. Multiple (polycystic disease)
3. Cystadenoma (proliferative)
4. Pseudocyst (degenerative; traumatic)
5. Teratomatous (dermoid)
6. Lymphatic (lymphangiomatous)
7. Endothelial (ciliated epithelium)

Parasitic cysts have been excluded from consideration in this study.

Boyd and others¹ believe that solitary hepatic cysts and polycystic liver disease are different manifestations of the same pathologic process. This opinion is, however, not generally held.

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Geist⁵ believes that multiple cysts are degenerative, arising from some abnormal extension of the resorptive process which occurs normally during the formation of bile ducts. Moschowitz¹⁵ first advanced the theory of aberrant bile ducts and blood vessel growth, resulting in solitary cyst formation. Inflammatory processes causing strictures in otherwise anatomically normal bile channels; degenerative cysts secondary to trauma with resorption of necrotic tissue; and the exceedingly rare neoplastic cyst are also advanced as the etiologic basis for solitary hepatic cysts.

Over 60 per cent of cysts occur in the right lobe, of which the anterior inferior surface is the most common site. Twenty per cent occur in the left lobe, whereas 10 per cent are located in the quadrate lobe and a bilobar distribution occurs in 10 per cent. During expansion, depending on the growth pattern, a cyst may become intrahepatic, primarily a surface structure, or actually pedunculated. The cyst wall is usually thin and transparent, has a grayish blue color and often contains many dilated vessels. It has a low internal tension in contrast to hydatid cysts. Reported sizes vary from 1 to 40 cm. in diameter, and fluid contents of as much as 17,000 ml. have been reported.⁴ Microscopically the majority of the true cyst walls are composed of three distinct layers. The inner layer is cellular, lined with flat, cuboidal, or columnar epithelial cells; the middle layer is composed of collagenous fibers with few cells; the outer layer contains segments of bile ducts and islets of liver cells. Traumatic cysts have only a membranous wall without a secreting epithelial lining.

The contents of the cyst vary in color, consistency and composition according to etiology, lining membrane and prevailing pathologic state. Hemorrhage or infection provoke, of course, conspicuous changes in the contained fluid.

Multiple cysts ("polycystic disease") may be confined to the liver alone, but are more commonly associated with cysts of the kidneys.¹¹ Less frequently, associated cystic disease is observed in the lung, pancreas, spleen, ovaries, brain, pituitary, breast or peritoneum. Multiple cysts are more common in children and are not uncommon

monly associated with other congenital malformations such as harelip, cleft palate, spina bifida, cardiac lesions, polydactylism, meningocele, vesical anomalies, hypospadias, and omphalocele with malrotation of the gut.¹⁷

Solitary cysts have an incidence of 0.3 to 0.1 per cent of the general population, are more common in adults and show a predilection for the white race. They occur four times more often in the female than in the male. The youngest reported case was that of Witzel in 1880 in which prolongation of labor was due to a large solitary liver cyst in a newborn.¹⁷ The oldest case is that of an 82-year-old man.⁶ Age incidence differs with the pathology. Solitary cysts usually occur in middle life whereas polycystic disease is usually discovered coincident to renal disease whether of the early or the so-called "delayed" type.

AN ANALYSIS OF NINE CASES

Of the 242,576 admissions to Georgetown University Hospital between 1933 and 1957, a diagnosis of hepatocystic disease was made in 9 cases.

General data. The diagnosis was established at necropsy in 4 of the cases, biopsy confirmed a clinical suspicion in 2 cases, and in the remaining 3 cases the diagnosis was made at laparotomy (table 1). The age range was 7 months to 67 years, and 6 of the 9 patients were females. Of the 5 patients who expired, polycystic disease of the kidneys, associated with severe renal failure, was found at autopsy in 4. In the remaining fatal case the right lobe of the liver was largely replaced by multiple cysts, and death occurred following attempted resection. In the 2 cases identified by

TABLE 1
General data

Patient No.	Age	Sex	Color	Method of Identification	No. of Cysts	Status
	yr.					
1.	7 mo.	F	W	Laparotomy	M*	Expired
2.	48	M	W	Necropsy	M	Expired
3.	64	F	C	Liver biopsy	S	Well
4.	58	F	C	Liver biopsy	S	Well
5.	56	F	W	Necropsy	M	Expired
6.	33	F	W	Necropsy	M	Expired
7.	48	M	W	Necropsy	M	Expired
8.	39	F	W	Laparotomy	M	Well
9.	67	M	W	Laparotomy	M	Well

* M = multiple; S = single.

TABLE 2
Distribution of cysts

Patient No.	Location of Hepatic Cysts	Location of Other Cystic Lesions
1.	Entire right lobe	Few ovarian cysts
2.	Right lobe	Renal, bilateral
3.	Right and left lobe	None
4.	Right lobe	None
5.	Right and left lobe	Renal, bilateral
6.	Right lobe	Renal, bilateral
7.	Lower aspect of right lobe	Renal, bilateral
8.	Right and left lobe	None
9.	Right and left lobe	None



FIG. 1. Cut section of the gross specimen, showing large multiple cysts throughout the entire right lobe.

needle biopsy the patients have remained asymptomatic since simple aspiration, and in 2 cases identified at the time of laparotomy, multiple small cysts were mistakenly identified as metastatic carcinoma and their true nature appreciated only on attempted biopsy. In two instances, a solitary cyst was present; in the remaining 7 cases, multiple cysts existed.

Distribution of cysts. The right lobe was the site of the cystic disease in each of the 9 cases (table 2), whereas the cysts were located in the left lobe, as well, in 4 cases. The size of the indi-

TABLE 3
Pathologic findings

Patient No.	Color of Cyst Contents	Pathology	Chemical Analysis of Cyst Contents
1.	Yellow-mucoid	Flat epithelial lining; pericystic inflammatory reaction	Protein, 1.2 gm. %; pH, 7.0; negative for ova and parasites
2.	Yellow-clear	—	Eosinophilic amorphous material
3.	Yellow-clear	Cystic degeneration-mesothelial cells	Protein, 1.1 gm. %
4.	Chocolate	Cystic degeneration	Hematest for blood, positive; icotest for bile, negative; amebic culture negative
5.	Yellow-clear	—	None performed
6.	Cloudy white	Cystic formation, lined with thin fibrous wall	None performed
7.	Clear-mucoid	Cystic formation, low cuboidal epithelium	None performed
8.	Yellow-clear	Low cuboidal epithelial cells with thin fibrohyaline wall	None performed
9.	Serosanguineous	—	Fluid smear negative for bacteria and fungi; cultures negative

TABLE 4
Diagnostic studies

Patient No.	Roentgen Studies	Liver Function Studies
1.	RUQ* mass with displacement of organs caudad, elevation of diaphragm	Van den Bergh, transaminase, cephalin flocculation, alkaline phosphatase—normal
2.	Flat plate of abdomen normal; no IVP† due to uremia	None performed due to uremia
3.	RUQ mass moving colon to lower abdomen—polycystic kidneys questioned.	Prothrombin, Bromsulphalein—normal
4.	RUQ mass displacing hepatic flexure anterior and caudad	Cephalin flocculation, alkaline phosphatase, prothrombin, Bromsulphalein—normal
5.	Flat plate of abdomen normal; no IVP (uremia)	None performed due to uremia
6.	Stomach displaced anteriorly	None performed due to uremia
7.	Polycystic kidneys on IVP	None performed due to uremia
8.	Flat plate abdomen normal	Cephalin flocculation, Bromsulphalein—normal
9.	Flat plate abdomen normal	Prothrombin, cephalin flocculation—normal

* RUQ = right upper quadrant.

† IVP = intravenous pyelogram.

vidual cysts varied from 0.5 to 8.0 cm. in diameter (fig. 1). Associated cystic disease was found in the kidneys in 4 cases, and in the ovaries in 1 case.

Pathologic findings. Both the gross and microscopic study of available specimens indicated that in each case the cysts were of the simple retention variety. The cyst contents were described as "yellow-clear" in 4 cases, mucoid in 2, bloody in 2

and cloudy white in 1 (table 3). Chemical analysis of the cyst contents revealed little other than a measurable protein content and negative studies for bacteria and parasites.

Diagnostic features (table 4). Nonparasitic liver cysts often give rise to no symptoms and usually are compatible with good health and longevity. Preoperative or premortem diagnosis of cystic

disease of the liver is seldom made, as evidenced by a report of 28 cases with no antemortem symptoms in 20,000 consecutive necropsies.¹⁶

Symptoms are usually directly referable to the complications. Increasing size of the abdomen is the most frequent complaint. Occasionally a mass is palpable and it may be soft, cystic, hard or solid. Pressure on neighboring structures by an enlarging mass causes vague discomfort or symptoms of intermittent obstruction of the bile ducts, pylorus or small bowel. Associated jaundice has been reported, as has hydronephrosis.¹⁴ Sudden sharp pain over the liver area has been described in a few cases, and its cause explained on the basis of a sudden change in the intracystic content, due either to hemorrhage or infection. Rupture of a cyst or torsion of its pedicle may simulate an acute intraabdominal catastrophe,¹⁰ although 1 case has been reported where rupture and peritoneal spillage caused little discomfort.¹³

A high index of suspicion is required in the diagnosis of hepatocystic disease. However, when there is a gradual increase in abdominal size with a palpable mass which moves with respiration, and has usually been present for some time without symptoms, a hepatic cyst should be suspected. Correct diagnosis is aided by x-ray which in 50 per cent of solitary cysts showed definite hepatic abnormalities. The diaphragm may be elevated, and irregular calcifications may rarely be seen throughout the tumor. Liver function tests are almost consistently normal. There is 1 reported case of cholangitis in a polycystic liver involving the entire left lobe and two-thirds of the right lobe which presented with jaundice and ascites, rapidly progressive hepatic decompensation, coma and death.⁵

TREATMENT

Inasmuch as the diagnosis of hepatocystic disease is most often made at the time of laparotomy for an indeterminate upper abdominal mass, operative treatment is carried out at that time. Less frequently, emergency surgical intervention may be required because of spontaneous rupture of a simple cyst or because of hemorrhage with sudden enlargement.

In certain instances surgical treatment may be ill advised, examples of which include: (1) cases with multiple cysts involving both lobes; (2) asymptomatic single cyst, identified by needle biopsy; and (3) small asymptomatic cysts discovered incidentally.

The surgical treatment that is employed must be based on various considerations, including the status of the patient, and the size, location and number of cysts.

Aspiration is usually reserved for long standing, very slow growing cysts, situated deep within the liver substance. Poor surgical risks are well suited for this type of therapy. The major disadvantage of aspiration is the blind approach and possibility of recurrence.

Incision and drainage are commonly used if doubt exists as to whether the cyst is solitary or multiple, in a deep seated cyst which makes marsupialization technically impracticable, and in patients who pose a poor surgical risk for a more extensive procedure. Disadvantages include the danger of a biliary fistula and of reformation of the cyst.

Marsupialization is the most common treatment performed. It may be in the form of an internal cyst-enterostomy to the stomach or jejunum, or external marsupialization may be made to the anterior abdominal wall; the cyst is drained and packed and the packing is removed in 2 to 4 days, and drainage usually stops in 5 to 7 days. Some have advocated insertion of sclerosing solutions to destroy the lining and allow granulation tissue to form with gradual obliteration of the cystic sac.

Excision, either partial or total, is possible in many cases. It is generally agreed that complete excision is the treatment of choice. If a plane of cleavage can be found, the cyst usually shells out easily. However, if a cleavage plane cannot be found, excision becomes very difficult. Liver damage and excess blood loss are the limiting factors of this surgical procedure. The raw hepatic bed that remains after excision may be obliterated by suture, packed with gauze, or filled with a tampon of omentum.

The surgical mortality associated with operations for hepatocystic disease has shown a persistent decline over the years from 20 per cent in 1932 to 2.4 per cent in 1955. Morbidity is usually related to the development of a persistent draining sinus. Other complications are recurrence, extensive liver damage with hepatic failure, infection (operative or retrograde), and malignant change.⁷ Incidence of malignancy with this disease is less than 1 per cent, and statistically insignificant in relation to total liver malignancy in the general population. Deaths have been reported from shock induced by sudden release of

fluid content from a large cyst with resultant sudden intraabdominal pressure changes.⁴

SUMMARY

Case records and autopsy reports of all admissions to Georgetown University Hospital from 1933 to 1957 were reviewed. The findings in nine patients with hepatocystic disease are presented. The associated signs and symptoms, diagnostic studies and therapeutic considerations in non-parasitic cystic disease are discussed.

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EVISCERATION OF ABDOMINAL WOUNDS: FACTORS INFLUENCING INCIDENCE AND PREVENTION

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Evisceration indicates the protrusion of intraperitoneal contents into or through an abdominal wound, which of course is necessarily preceded by disruption of the wound closure. This term should be clearly distinguished from "wound dehiscence" or "separation" which terms imply separation of one or more layers of the wound without protrusion of intraperitoneal contents.

Inasmuch as one of us (E. B. B.) has had the unique experience of encountering no instance of evisceration in a surgical experience spanning 10 to 12 years, all cases of abdominal wound evisceration encountered at Georgetown University Hospital from 1947 to 1957 have been collected and analyzed in regard to factors influencing the incidence of this distressing complication. In addition, comparisons have been made between various technical methods employed in wound closure in these cases on the one hand, and the routine measures utilized in a large series of cases in which this complication had not occurred.

GENERAL FACTORS

During this 10-year period, 43 cases of evisceration occurred, representing an incidence of 0.003 per cent, and many more cases of dehiscence or separation were encountered. The majority of the patients were of advanced age, 77 per cent being over 40 years. However, evisceration occurred in the case of a 1-year-old child. Although a high male incidence is usually reported,¹ 67 per cent of this group occurred in women. No racial or color predisposition to evisceration was noted in this study. The average time of evisceration, and this is also true of dehiscence, was on the 8th postoperative day; this varying from the 5th to the 30th postoperative day. Not infrequently the patient volunteered the information that "something had burst" after coughing, vomiting or straining. Not long thereafter, a serosanguineous

drainage from the incision took place; this was observed in almost one-half of our cases.

CONTRIBUTING FACTORS

It is clearly evident that in addition to purely technical and local factors, various constitutional or systemic influences have a very important relation to the incidence of wound evisceration.

Constitutional factors. The role of the constitutional factors has been assessed in these 43 cases (table 1). Either abdominal distention, nausea and vomiting, or coughing complicated the early postoperative period in the majority, whereas anemia, the presence of neoplastic disease, and hypoproteinemia existed with significant frequency. The fatal outcome in 7 cases, representing a 16.2 per cent mortality, is indicative not only of the serious import of evisceration but also of the depleted status of many of these victims. The influence of intense steroid therapy upon evisceration is difficult to estimate, and in none of our cases was a direct relationship evident.

Closure and care of the incision are undoubtedly the final determinants of wound integrity. It is undoubtedly true that evisceration probably begins with the protrusion of a small amount of intraabdominal tissue through an aperture in the peritoneal closure. Factors that interfere with normal wound healing are excessive foreign material and tissue necrosis. Although bacterial contamination has been similarly accused, it is noteworthy that purulent infection and evisceration are rarely associated. To insure secure healing, the tissues must be handled gently, there must be adequate hemostasis, fine sutures must be used in the wound, and the tissues must not become dehydrated. One of the most common mistakes is to tie the sutures too tightly, thus devascularizing the tissues.

Type of operation. The type of operative procedure probably influences evisceration only insofar as related malignant disease and the location of the involved incision influence wound healing (table 2). The fact that almost one-half of our series occurred after gynecologic operations

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TABLE 1
Constitutional factors in evisceration

	No. of Cases	Per Cent
Distention.....	25	58
Nausea, vomiting.....	14	32
Atelectasis.....	3	7
Cough.....	13	30
Pneumonia.....	5	11
Anemia.....	22	51
Carcinoma.....	11	25
Hypoproteinemia (protein below 5.6 gm./100 ml.).....	8	18

TABLE 2
Type of operation

	No. of Cases	Per Cent
Gynecologic.....	21	49
Gastrectomies.....	4	9
Biliary.....	8	18
Colon.....	5	12
Miscellaneous.....	5	12

TABLE 3
Type and location of abdominal incision

	No. of Cases	Per Cent
Upper abdomen.....	17	39
Upper right rectus.....	11	25
Upper left rectus.....	3	6
Thoracoabdominal, left rectus.....	1	2
Transverse.....	2	4
Lower abdomen.....	26	61
Lower midline.....	17	39
Lower right rectus.....	4	9
Lower left rectus.....	5	11

probably relates to the common use of the low midline incision. The *type and location of the abdominal incision* appears to influence importantly the incidence of evisceration (table 3). The transverse or oblique incision is inherently stronger than a ventral one. Although it is commonly claimed that the upper abdominal incision is more prone to evisceration, 60 per cent of this series were associated with a lower abdominal incision.

The majority of wounds in this series were closed in layer with chromic catgut (table 4). However, the relative incidence of cases of evisceration

TABLE 4
Technique of wound closure

	No. of Cases	Per Cent
In layer with chromic catgut.....	25	58
In layer with nonabsorbable sutures.....	9	21
In layer with retention sutures.....	9	21

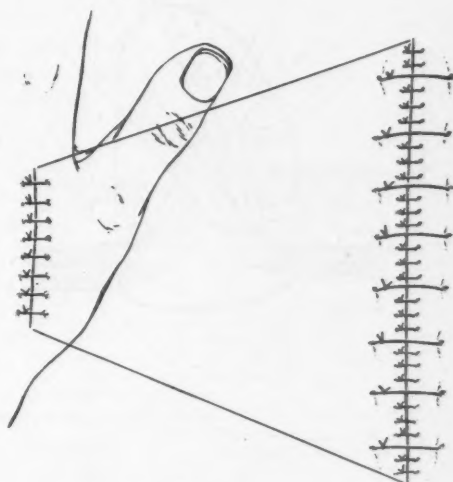


FIG. 1

ceration closed with catgut *versus* nonabsorbable suture material represents, approximately, the relative popularity of these suture materials in our institution. In no case was evisceration associated with a frank wound infection. In this series, the employment of a drain did not seem to promote evisceration. Premature removal of the skin sutures may permit the development of evisceration in a wound that otherwise might eventuate merely in an incisional hernia. It is significant that the skin sutures had been removed on or before the 7th postoperative day in 44 per cent of our cases. Although retention sutures were employed in a considerable number of these cases, it should be pointed out that an average of only three such sutures per incision was employed.

FACTORS RELATING TO THE PREVENTION OF EVISCERATION

To prevent evisceration, routine employment of various prophylactic measures is mandatory.

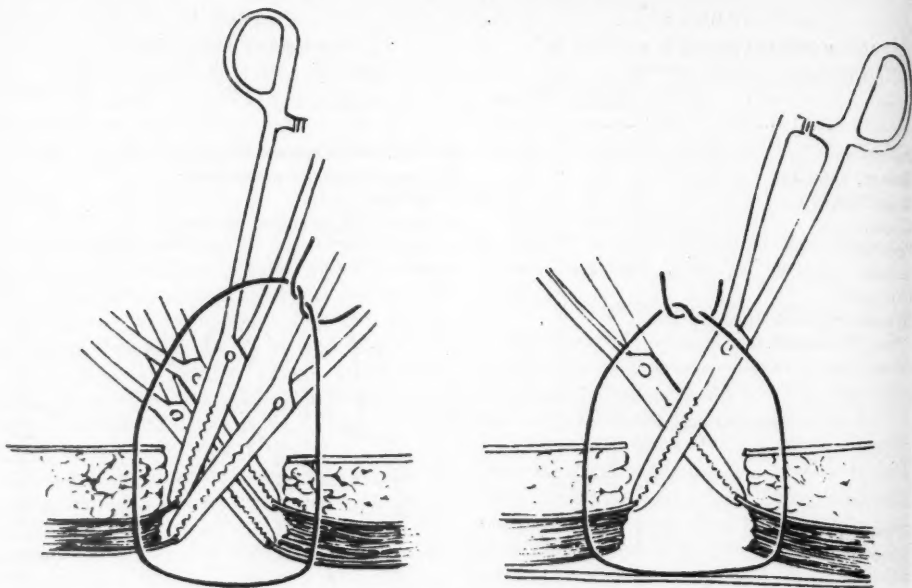


FIG. 2

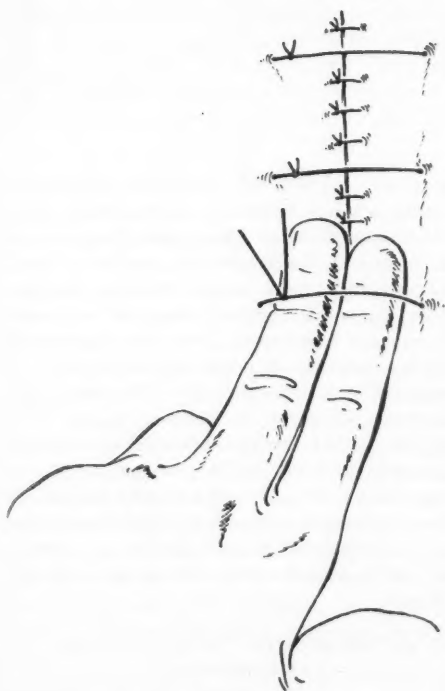


FIG. 3

Anemia and hypoproteinemia should be corrected as far as possible before major surgery is undertaken, and it is equally important that they be controlled postoperatively. Chronic pulmonary disease should be treated in the preoperative period, and routine measures directed toward the avoidance of postoperative pulmonary complications should be exercised. The routine use of the nasogastric tube with continuous suction should be instituted in all cases in which paralytic ileus can be anticipated, and oral feedings should be withheld until peristaltic activity is audible on auscultation.

The proper use of retention sutures in the closure of the abdominal incision is, in our opinion, the most important single factor in the prevention of eversion. Kennedy³ reported that in a 56-year experience, which included 30,000 cases, he failed to encounter a single case of eversion with properly placed through-and-through retention sutures. Although the routine use of retention sutures has been objected to by Whipple and Elliott,⁶ on the premise that this technique predisposes to infection, others have stressed the value of retention sutures in the prevention of eversion. Reid and associates⁷ described the use of through-and-through silver wire sutures for closure of the abdomen in acute

abdominal emergencies, and encountered no evisceration in 334 cases. Holman and Eckel in 1941,² using wire retention sutures, observed no incidence of evisceration.

The authors employ through-and-through retention sutures of either wire or silk, using 6 to 10 in the average incision. The proper spacing of these retention sutures can be determined by projecting to the abdominal incision the spacing of skin sutures in a small subcutaneous incision (fig. 1). The incision is then closed in layers and the tension sutures tied without undue tension. Whether the through-and-through sutures are placed into the abdominal cavity or down to the peritoneum (fig. 2), depends principally on the preference of the operator. The sutures are tied over two fingers of the assistant, thus preventing the cutting of the skin as the result of postoperative edema (fig. 3). Premature removal of skin sutures is to be avoided. Nelson and Dennis⁴ have pointed out that the maximal increase in tensile strength in normally healing abdominal wounds in animals occurs from the 7th to the 16th day. It is our practice to remove skin sutures not earlier than the 9th day and tension sutures on the 14th postoperative day.

The use of this type of closure is recommended in (1) patients undergoing gastrointestinal surgery, (2) debilitated cases and those with malignant disease, (3) patients over the age of 40, (4) patients with intraabdominal infection and (5) patients in whom one might suspect faulty wound

healing. No single case of evisceration has been observed using this technique of wound closure.

SUMMARY

Forty-three cases of evisceration have been reviewed from the standpoint of the factors influencing both the occurrence and prevention of this complication. A technique of wound closure, utilizing retention sutures, is suggested as a completely effective safeguard in preventing evisceration.

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HYPERPARATHYROIDISM AND CHRONIC CALCIFIC PANCREATITIS

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The fact that the relationship of hyperparathyroidism to inflammatory disease of the pancreas is more than coincidental has been recently pointed out by Cope and associates.¹ A review of the literature revealed 10 cases involving this association, in 7 of which calcific deposits were demonstrated within the pancreas. In a discussion of Cope's paper, Rienhoff reported 2 such cases of calcific pancreatitis in association with hyperparathyroidism while Smith and Cooke⁹ and Page,⁶ each reported a single similar case. Rogers and co-workers,⁸ in reporting a case of healed duodenal ulcer in association with "water-clear cell" hyperplasia of the parathyroid glands, called attention to the presence of calcific material within the pancreas. In the cases of Dawson and Struthers,² and Martin and Canseco⁴ the calcific deposits were observed in various tissues throughout the body as well as in the pancreas. The co-existence of hyperparathyroidism and acute hemorrhagic pancreatitis has been observed in 2 cases, and in a single case chronic relapsing pancreatitis occurred with hyperparathyroidism. In these 3 latter cases roentgenologic evidence of calcific disease of the pancreas was lacking. Although it is not entirely clear, the case histories in most of these instances indicate that the symptoms of hyperparathyroidism antedated the development of symptoms referable to the pancreas. The obvious implication is that as a result of the pre-existing hyperparathyroid state, the disturbed calcium metabolism resulted in a precipitation of calcium salts within the pancreatic ductal system with formation of intraductal stones. As a result of blockage of the ductal system by these calculi, subsequent attacks of acute pancreatitis developed. In the few cases in which the pancreatic disease was of a noncalcific type the mechanism is less clear. However, it has been suggested that significant amounts of calcium in the pancreas may escape roentgenologic detection.

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In view of the relatively few reported cases, and because of its several unusual features, the following case is reported in detail.

CASE REPORT

History. G. F., a white man aged 37, was first admitted to Georgetown University Hospital on August 6, 1953, because of a generalized atopic dermatitis. A cataract had been removed from the right eye 1 year previously. A history of alcoholism of 3 years' duration was obtained. Liver function tests at that time were within normal limits. A serum calcium level of 11 mg. per cent was noted. However, the serum phosphorus and alkaline phosphatase determinations were within normal limits.

At the time of the second admission, on November 17, 1954, a history of an attack of upper abdominal pain 3 months previously, diagnosed on hospitalization elsewhere as acute pancreatitis, was obtained, and it is noteworthy that an elevated serum calcium was found at this time. The dermatitis had been well controlled by treatment with cortisone and adrenocorticotrophic hormone (ACTH). A roentgenogram of the abdomen revealed the presence of calcific shadows overlying the liver area. Calcification of the pineal gland was observed on roentgenogram of the skull. Pertinent laboratory data include: serum calcium, 10.2 mg. per cent; serum phosphorus, 3.2 mg. per cent; Sulkowitch test, negative; bromsulfalein, 40 per cent dye retention.

On June 2, 1955, this patient was readmitted because of an attack of acute upper abdominal pain of 6 hours' duration. The serum amylase determination was 101 units. A discharge diagnosis of acute gastroenteritis was made.

His fourth admission, on August 26, 1955, was required because of recurrent upper abdominal pain. At this time mildly elevated serum amylase levels of 133 and 130 units were obtained, establishing the diagnosis of acute pancreatitis. Bromsulfalein determination revealed 5 per cent dye retention, and the cephalin flocculation was 2+.

A recurrence of upper abdominal pain led to readmission on January 8, 1956, at which time the serum amylase level was 150 units. A blood fat curve, obtained after the administration of ¹³¹I tagged triolein, showed moderate flattening indi-

ating significant pancreatic dysfunction. The serum calcium level was 13.0 mg. per cent, and serum phosphorus, 3.5 mg. per cent. The serum amylase level was 150 units. During this period of hospitalization an abrupt fall of hematocrit from 42 per cent to 31 per cent was associated with the passage of several tarry stools. An upper gastrointestinal x-ray study failed, however, to reveal the presence of a peptic ulceration.

Readmission for the sixth time, on August 25, 1956, was for the purpose of a complete survey of his apparent idiopathic hypercalcemia. Significant laboratory data included: serum calcium, 10.1 mg. per cent; serum phosphorus, 3.5 mg. per cent; tubular resorption of phosphorus, 97.6 per cent; and the 24-hour urinary excretion of calcium on 150-mg. calcium diet was 320 mg. and 260 mg. on two occasions. The hypercalciuria was attributed at this time to the continuous cortisone therapy that this patient had received over a period of 5 years for his atopic dermatitis. The simultaneous occurrence of an elevated tubular resorption of phosphorus and hypercalciuria seemed an inexplicable paradox at that time. However, it is now well established that Amphogel, which he was using because of prolonged steroid therapy, and a restricted calcium intake, limited to 150 mg. daily during that period, may effectively convert the tubular resorption of phosphorus to normal or elevated levels in the presence of hyperparathyroidism. An intravenous cholecystogram revealed a normal gall bladder as well as localized calcification in the liver or extrahepatic bile ducts (fig. 1).

On August 26, 1957, he was again admitted to the hospital because of an exacerbation of his pancreatitis. Serum amylase level was 320 units. A flat plate of the abdomen revealed for the first time calcific shadows in the region of the pancreas (fig. 2).

Another recurrence of the acute pancreatitis required hospitalization on June 15, 1958, at which time the leukocytes were 25,000 and serum amylase, 204 units. After subsidence of the acute symptoms, additional metabolic studies were carried out. Serum calcium was 12.2 mg. per cent; the serum phosphorus, 3.4 mg. per cent and the tubular phosphorus resorption, 80 per cent. During this later study, a regular diet with generous milk content was designed to supply an adequate phosphorus intake, and in addition, antacid therapy was stopped 5 days previously. Slight osteoporosis of the lumbar spine was demonstrated by x-ray. An eye consultant noted the presence of calcific deposits in the fornix in the lid border of the left eye. In addition a lens cataract was observed. A 24-hour urinary excretion of calcium on 150 mg. intake was 347 mg. per cent. At this time it was



FIG. 1. Intravenous cholecystogram with intrahepatic calcification above the gall bladder.



FIG. 2. Calcific deposits in region of head of pancreas, and in addition, calcification within liver.

felt that a diagnosis of hyperparathyroidism was more clearly evident. Following discharge, repeated outpatient studies revealed the serum calcium ranging from 11.2 to 13.6 mg. per cent, and the serum phosphorus from 2.6 to 3.2 mg. per cent.

On October 26, 1958, he was admitted for surgical exploration of the parathyroid glands. The preoperative phosphate clearance was elevated.



FIG. 3. Adenoma of right upper parathyroid

Because of the prolonged use of cortisone, steroid therapy was introduced preoperatively and continued during and after the operative procedure. On surgical exploration of the left parathyroid area, the upper and lower parathyroid glands were of normal size, and both were biopsied. The right inferior parathyroid gland was normal, and it too was biopsied. The right upper parathyroid gland was the site of a tumor, measuring 2 by $1\frac{1}{2}$ by 0.4 cm. which was removed (fig. 3). A nodule, measuring 0.5 by 0.25 cm., was found in the isthmus of the thyroid gland. The isthmus was resected. Pathologic examination of the tumor of the right upper parathyroid gland revealed it to be benign chief cell adenoma. Biopsies of the other three parathyroid glands revealed normal structure. The nodule of the isthmus of the thyroid gland was found to be a papillary adenocarcinoma.

Postoperatively an immediate drop in serum calcium to 9.1 mg. per cent was observed. The serum phosphorus remained at a level of 3.3 mg. per cent in the immediate postoperative period, a delayed rise to 4.7 mg. per cent occurring on the 4th postoperative day. As soon as liquids were tolerated on the 1st postoperative day, a generous supply of milk insured an adequate phosphorus intake. The immediate postoperative phosphorus clearance was 0.8, a hypoparathyroid level. Subsequently, the phosphorus clearance rose to 8.7, 10 and finally 14. He was discharged from the hospital on the 14th postoperative day.

DISCUSSION

As has been previously pointed out, an awareness of the association of hyperparathyroidism and inflammatory disease of the pancreas is important in that it may be helpful in the diagnosis of the former condition. Apart from the symptoms stemming from the complications of hyperparathyroidism, namely renal calculi, peptic ulcer syndrome, psychoneurotic symptoms, the loss of

renal concentrating ability, and the rather rare occurrence of clinically evident osseous disease, the symptoms of hyperparathyroidism *per se* are notably obscure and vague.

Although it is impossible to state at this time the frequency of pancreatic complications occurring during the course of hyperparathyroidism, it is not unreasonable to believe that the number of reported cases represents only a small fraction of the actual cases. In a review of our material and in other surveys the finding of calcification in various sites throughout the body in association with calcific pancreatitis has been repeatedly noted. The more common of these sites are the prostate, the genitourinary tract, conjunctiva and liver. In our case, calcification was observed within the liver, in the pineal gland and in the conjunctiva. In addition, a cataract had been removed from one eye and one intercurrently developed in the other. These lenticular changes were considered a manifestation of the chronic atopic dermatitis rather than of hyperparathyroidism.

Serum calcium and phosphorus determinations have not been routinely employed in the study of calcific pancreatitis in the past. However, in a review of our cases it has been noted in several that a significant elevation of the serum calcium was present. Inasmuch as a depression of the serum calcium not infrequently accompanies acute pancreatitis, or an acute exacerbation of chronic pancreatitis, a normal serum level may provide false evidence concerning both hyperparathyroidism and the hypocalcemia of pancreatitis. It is significant that at the time of the initial hospitalization of this case, 5 years before the establishment of the correct diagnosis, a mild degree of hypercalcemia was found. However, the normal serum phosphorus at that time did not lend support to a diagnosis of hyperparathyroidism.

Various pathologic and clinical features of calcific pancreatitis suggest the possibility of a not uncommon relationship with hyperparathyroidism. Although it has been repeatedly stated that in the majority of cases of calcific pancreatitis there is a deposition of calcium salts in the parenchyma of the gland as a result of previous inflammation, our studies indicate that the calcific material is invariably intraductal in location. Similar findings were reported by Peters and associates⁷ in a study of 41 cases of calcific pancreatitis. Fur-

thermore, many cases of calcific pancreatitis are asymptomatic and in many other instances calcific material in the pancreas is observed at the time of the initial attack of abdominal pain. These facts suggest that rather than being the result of acute recurrent attacks, the calcific intraductal collections provoke acute pancreatitis as a result of obstruction of the ductal system.

It is not illogical to suspect that some factor other than inflammation may be operative in the causation of calcification within the pancreas. Edmondson and associates,³ in an extensive consideration of the pathogenesis of intraductal and intrapancreatic calculi, point out that the stones are invariably made up of calcium carbonate or calcium phosphate. Analysis of the stones in our cases confirms this fact. They point out that as a result of the normal concentration of calcium and phosphorus in pancreatic juice, the precipitation of calcium carbonate or phosphate to form calculi in the ducts of the pancreas can be readily explained in considering the various factors, both real and theoretical, that may provoke this precipitation. No mention is made, however, of hyperparathyroidism in this regard.

The recognition of associated hyperparathyroidism is of obvious importance in the treatment of chronic calcific pancreatitis. Since our present therapeutic efforts in calcific pancreatitis should, in our opinion, consist of surgical removal of the intraductal calculi, the presence of unrecognized hyperparathyroidism would undoubtedly result in reformation of these stones. The question of the dissolution of already existing calculi after correction of the hyperparathyroid state is unsettled at the present time. If, as suggested by Edmondson and co-workers,³ small concretions are commonly passed out of the pancreatic ductal system, removal of the larger obstructing concretions by surgical means after elimination of the hyperparathyroid state may result in passage of the smaller calculi.

It is abundantly clear that a careful screening of all cases of calcific pancreatitis for chemical

evidence of hyperparathyroidism should be carried out. Owen and Howard,⁵ in reporting 32 cases of pancreatic calcification, state that in no case was there evidence of a parathyroid tumor. However, more detailed information than is provided by a single serum calcium and phosphorus determination is necessary in order to exclude this condition, as evidenced by the data relating to this reported case.

SUMMARY

The collected cases of associated hyperparathyroidism and calcific pancreatitis are analyzed. A detailed report of an additional case is made. Factors relating to the mechanisms involved in this complication of hyperparathyroidism are considered.

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A SIMPLIFIED EXTRACORPOREAL PUMP OXYGENATING SYSTEM*

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Numerous devices have been described for the extracorporeal oxygenation and pumping of blood. Many of these have been complex in construction and operation, limited in oxygenating capacity or associated with excessive changes in blood elements during the bypass. A simplified pump oxygenator has been designed which can be safely operated with minimum of personnel and which still fulfills the requirements of adequately pumping and oxygenating large amounts of blood. This apparatus is operated with purely mechanical controls. Electrical power is needed only for monitoring and temperature control since the pumping mechanism is activated entirely by compressed gas under regulated pressures. The pumping device utilized in this system has been used and tested in the laboratory and clinic during the past 2 years, and has been extremely satisfactory. A schematic representation of the pump oxygenating system is given in figure 1. Each of the components of this system will be described separately in the order in which they are used in the circuit as blood passes from the cavae through the system and is returned to a peripheral artery.

Blood is withdrawn by gravity from the cavae or the auricle by means of catheters in the usual way. It then passes individually from the superior and inferior cavae to two inlets on the flowmeter. The flowmeter itself consists of two cylinders, 8 inches in height, connected by an inclined spillway (fig. 2). Blood thus passes from the higher cylinder into a lower one through an orifice which is graduated in width from the bottom to the top. As blood passes through this chamber the height of the column in the proximal cylinder indicates the rate of flow. The flowmeter is positioned to lie 12 to 18 inches below the level of the auricle. The size of the orifices permits the passage of 5 L. of blood through this flowmeter without sig-

nificant delay. The outlet of the flowmeter is mounted well above the top of the oxygenating column, and the height of the flowmeter can be changed by moving it up or down along its mounting. With increasing experience we have felt the need for a venous flowmeter to be less than in the early stages of development of the apparatus. However, it has been helpful in obtaining a constant reading of the flow rate throughout periods of bypass and enables one to ascertain the occurrence of problems which might otherwise be momentarily overlooked.

The oxygenator is of the double concentric column bubble type, and is 27 inches in height. The base plate of the oxygenator and all of the fittings are of nylon. The columns and exterior shell are of a treated Plexiglas which is autoclavable. The entire unit is therefore transparent and sterilizable by heat. Blood is admitted through the inner oxygenating column through a central opening. The base plate is perforated for the admission of oxygen. An additional central tube of nylon extends three-fourths of the distance up the inner column in a central location. This central tube also supplies oxygen through small radial holes arranged in a spiral throughout the length of the tube (fig. 3). This central oxygen tube greatly increases the oxygenation of the blood over that which is obtained by the admission of oxygen through the base plate alone. The top portion of the outer chamber is enlarged, the upper chamber and the upper two-thirds of the lower portion are filled with siliconized steel mesh. Blood passes up through the central oxygenating tube until it reaches the top; as it overflows it trickles downward through the siliconized steel mesh into the lowermost portion of the outer chamber which forms a reservoir. The blood level in this reservoir is kept sufficiently high to include the lowest portion of the siliconized steel mesh so that there is no free fall of blood from the mesh into the reservoir. Anti-foam "A" is the debubbling agent used on the mesh. Before

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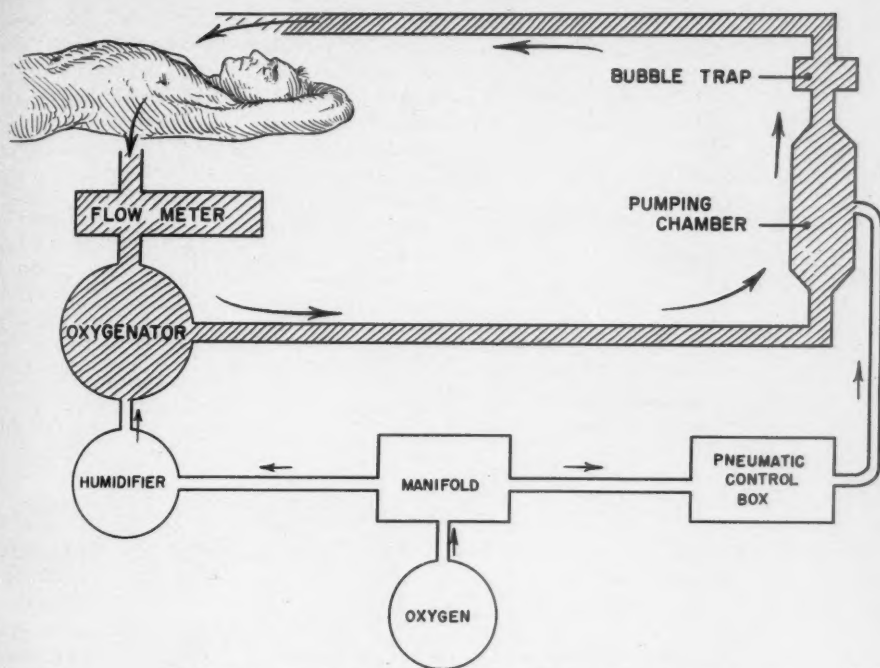


FIG. 1. Diagrammatic scheme of simplified pump oxygenator

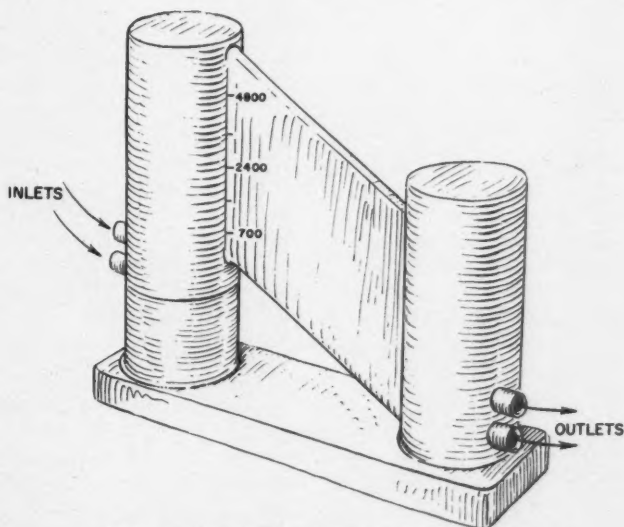


FIG. 2. Venous flowmeter with inclined spillway

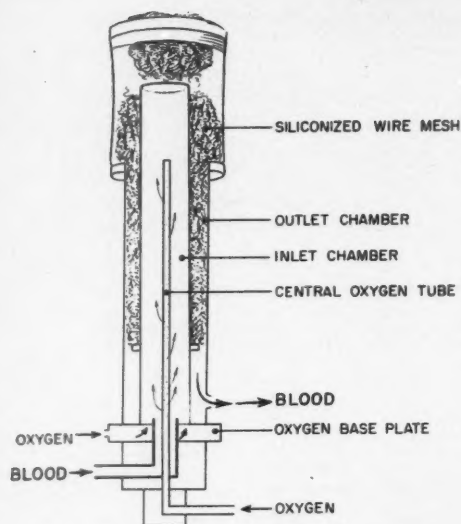


FIG. 3. Vertical section through oxygenator

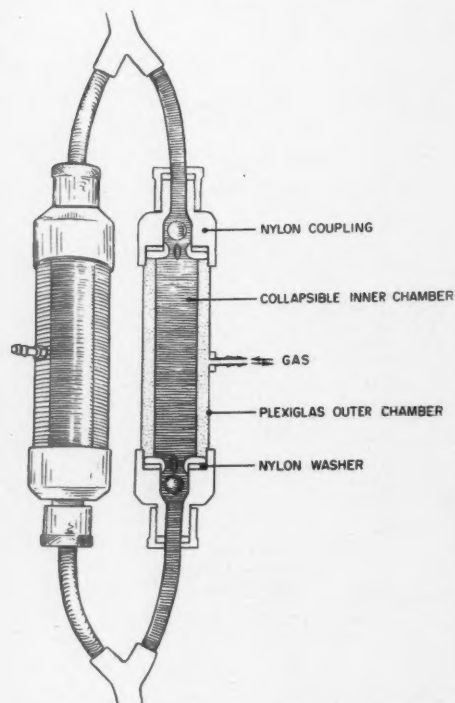


FIG. 4. Pneumatic pumping units coupled to a single outlet, showing a vertical section through one unit.

use, the mesh is thoroughly washed and chemically cleaned. This is followed by the application of the Anti-foam "A" which is then allowed to dry. After drying, the steel mesh is again thoroughly washed with water and heated. It is then assembled in the oxygenator where it is sterilized by autoclaving. Blood is withdrawn into the pumping unit through the opening in the base plate at the base of the reservoir. The assembled oxygenator is diagrammatically shown in figure 3. The oxygen mixture employed is $1\frac{1}{2}$ per cent carbon dioxide with $98\frac{1}{2}$ per cent oxygen. The oxygenating capacity of this unit is 5 L. per minute.

Pumping is accomplished by utilizing the principle of the rapid introduction and evacuation of air round a compressible inner chamber enclosed within a rigid compartment. Each of the pump-



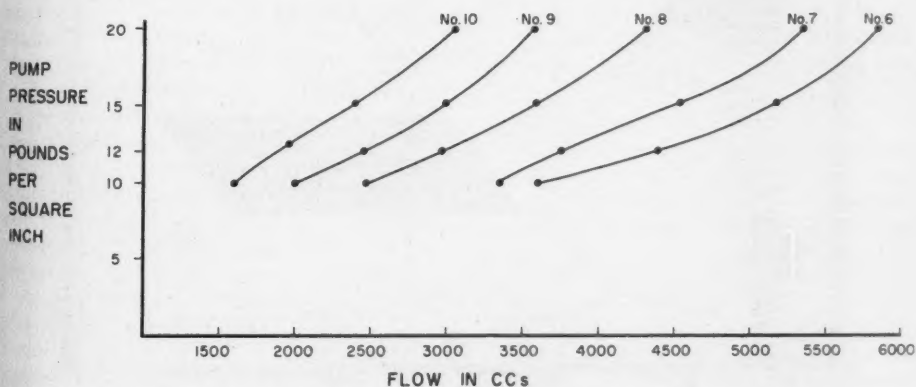
FIG. 5. Pneumatic pump "ventricle" in position of ejection.

ing units is composed of these two parts. These are an outer rigid cylinder of treated Plexiglas and an inner compressible chamber of Silastic (silicone rubber) which has a ball valve incorporated into each end to produce unidirectional flow of blood. The compressible chamber which is filled with blood is held within the walls of the outer rigid cylinder. Compressed gas is then admitted by a valve to the space between the walls of the two chambers. Thus when gas is admitted, the Silastic unit is compressed and expels the blood which was contained within its lumen. The gas is rapidly evacuated, releasing the pressure as blood flows from the intake side to fill the compressible chamber again. Figure 4 shows the schematic diagram illustrating the pumping chambers. In this illustration two such chambers are coupled to a single arterial outlet. If gas is admitted simultaneously to each chamber, both eject blood and refill at the same time. It is more satisfactory to alternate the compression of these units so that a relatively continuous flow of blood is obtained but which still maintains a pulse wave. Figure 5 shows such a unit in the state of compression. Ball valves in each end of the pumping chamber are an integral part of the pumping unit. The balls of the valves can be removed for cleaning. The capacity of each pumping chamber

is 75 cc. The amount of blood which is ejected with each stroke is determined by the pressure admitted within the Plexiglas chamber. The output of the pump is predictable, based upon the pressure and the rate of compression. This is controlled through the central control unit which will be described in another section of this paper. The pressures customarily employed vary between 10 and 20 pounds. A table of outputs is given in graph 1. The stroke output per pumping unit can be varied from 0 to 45 cc. Thus using two pumping units the theoretic output would be 9000 cc. per minute. The resistance imposed by a relatively small arterial catheter imposes a limitation of the output to approximately 5800 cc. per minute when a size 5 Teflon catheter is used. If larger catheters are used the theoretic output can be achieved.

Pumping is activated by the pneumatic control unit. The single pneumatic control unit can be employed to regulate from 1 to 4 pumps. A source of compressed gas with a pressure of at least 40 pounds per square inch is utilized for the operation of all pumping chambers. By using an excess pressure in the input line, variations in pressure due to escape of gas at the exhaust cycle are minimized. A control valve and gauge on the input side of the control unit adjusts this input

FLOW RATE OF 2 HUFNAGEL PUMPS (ALTERNATE) AT VARIOUS PUMP PRESSURES
AT 80 CYCLES PER MINUTE



DELIVERED AT TABLE-HEIGHT, WITH LINE RESISTANCE ONLY WITH TEFLON CANULAE
OF VARIOUS SIZES. -- JAN. 23, 1959

GRAPH 1.

Flow rate of two Hufnagel pumps (alternate) at various pump pressures at 80 cycles per minute.

pressure to a constant level. There are four outlets from the pneumatic control regulated by two gauges. Each gauge is connected to a pair of outlets. Each of the two outlets associated with a single gauge alternately produce equal pressures. Thus in figure 6, which shows the control unit, a gauge to pump "A" controls the two outlets associated with it. Pump "B" does the same for its paired outlets. By attaching both ventricles to the same pump, alternate compression is obtained. By connecting one ventricle to pump "A"

and one to pump "B" both ventricles can be made to eject simultaneously. In practice we have used the alternate method to even out the variations in flow and to secure a maximal output without building up excessive pressures within the arterial line. This leaves a reserve unit which can be connected for emergency in case of mechanical failure of the other unit. The pressure in each of these two systems can be regulated independently through the valve controls as shown in the photograph. The rate of pumping is also regulated be-

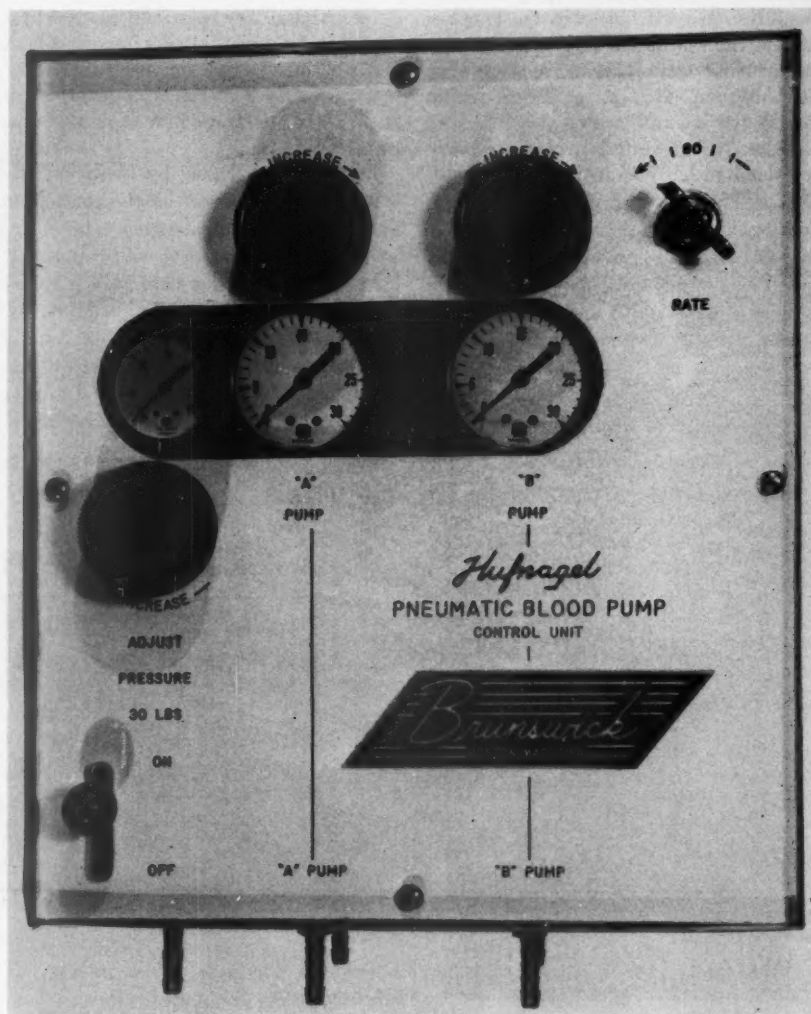


FIG. 6. Control unit; inlet for entire unit is at left. Four outlets for separate pumping units are shown under "A" and "B".

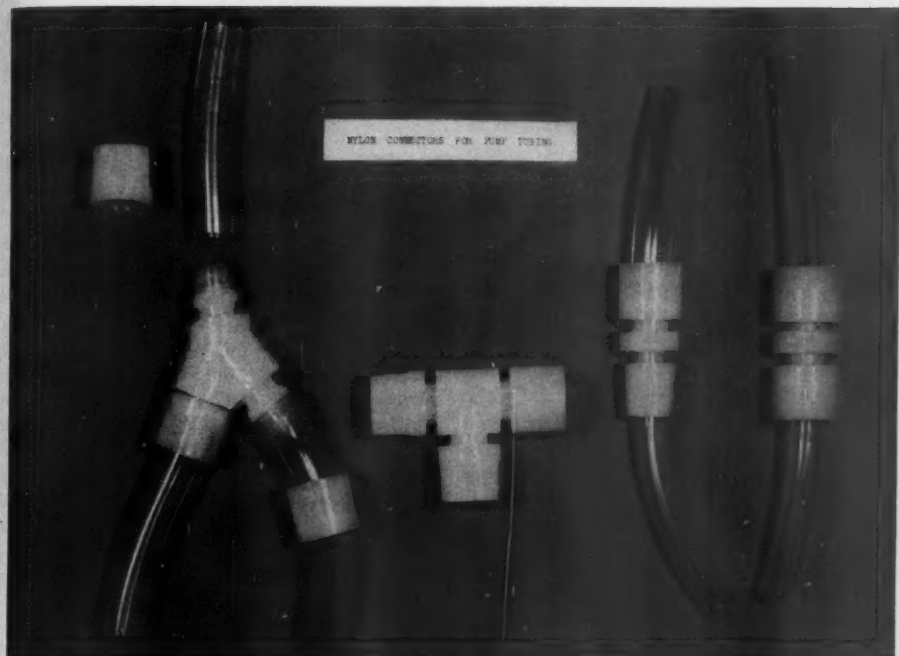


FIG. 7. Nylon connectors showing type of nonslip junctions

tween 50 and 100 strokes per minute. If it is desired to vary the pressure between the two ventricles this can be accomplished by attaching one ventricle to pump "A" and one ventricle to pump "B." This great versatility of being able to obtain either simultaneous or alternate compression of the ventricles and either single or dual control of the pumping pressure greatly adds to the functions to which the unit can be used.

The tubing leading from the pumping ventricles then passes to the arterial catheter. It has been helpful to interpose a small T-tube in the arterial line from which any small air bubbles, admitted to the tubing at the time of insertion into the artery, may be removed. If a heat exchanger is utilized, this T-tube need not be employed.

As in all oxygenating units the desirability of maintaining tight fitting junctions at all connections has been emphasized. To maintain this and laminar flow at junctions, special connectors have been designed. These are made of nylon and have screw caps to prevent displacement of the tubing and the ensuing complications. Figure 7 shows the method of stretching of the Tygon tubing

over the end of the nylon connector and the use of the screw type caps to exert sufficient pressure to prevent dislodgment. These connectors are made in various sizes with step-up and step-down ends so that different sized tubing can be utilized. All tubing in this pump oxygenator is $\frac{3}{8}$ or $\frac{5}{8}$ inch in diameter. When these connectors are utilized it is impossible to dislodge the tubing from the connector even by forcible pulling on the tubing.

DISCUSSION

A basic simple type pump oxygenating system has been evolved. The use of the pneumatic type pumping unit minimizes trauma to the blood during pumping and allows accurate control of the amount of blood being pumped. The use of a dual unit with individual controls gives an additional factor of safety.

Each of the pumps in use gives sufficient output to maintain perfusion in the event of failure of one of the units. The utilization of two pumping mechanisms independent of each other within the same control unit gives a further safety factor. The regulation of the pressure within the pumping chamber permits accurate control of

the stroke volume. Mechanical control eliminates the use of electrical power sources. The use of two pumping units in alternating cycles minimizes turbulence and permits high outputs without the development of excessive pressures proximal to small intraarterial catheters. When this pump oxygenating unit is employed bypass oxygenation can be maintained at normal levels. Following a 1-hour perfusion in dogs, serum hemoglobin levels averaged under 20 mg. per cent per hour. The total priming volume necessary to fill the apparatus is 1200 cc. Additional controls such as level sensing devices to control the level of the blood in the oxygenator have been used, but we have found their value limited.

Other apparatus such as a heat exchanger can be readily incorporated into the unit. The return of coronary suction or left heart decompression blood into the unit is simple. The unit has been employed for infants and adults, utilizing high

rates of perfusion with normal temperatures and lower rates of perfusion with hypothermia.

SUMMARY

A simplified pump oxygenator system has been described which permits good oxygenation with high flow rates, minimal trauma to the blood and which is simple to operate. The oxygenating unit is transparent and completely autoclavable. The pumping unit is efficient and atraumatic. The priming volume is low and its output is variable between 500 and 5000 cc. per minute.

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DIRECT APPROACHES FOR THE TREATMENT OF AORTIC INSUFFICIENCY*

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Extensive studies of the pathology of the aortic valve have delineated more accurately the types of anatomic deformity which produce aortic insufficiency.^{3, 5} Rheumatic fever and luetic valvular disease have long been considered the primary causes for the development of this lesion. With changing conditions and improving antibacterial and antiluetic therapy other forms of the disease have become increasingly prominent. Since there is a correlation between the origin of a lesion and the usual anatomic type of the deformity producing the insufficiency it is of importance to review this relationship.

1. *Trauma.* Direct penetrating wounds, particularly knife wounds, can produce the acute lesion of clean section of a leaflet. Nonpenetrating trauma, particularly blast injury or steering wheel injury leads to avulsion of one or more cusps.

2. *Acute endocarditis.* Destruction of the body of a cusp by erosion of a leaflet is a common form of this lesion. Not infrequently a single cusp is involved and fenestration of the cusp may occur with preservation of the margin.

3. *Subacute bacterial endocarditis.* This lesion can produce aortic insufficiency of varying degrees. The deformity of the cusp or cusps may be associated with a destructive process in which case a rather acute aortic insufficiency is produced during the course of the early phases of the process. A second variety is that associated with the scarring of one or more cusps during the healing phase of antibiotic therapy. This lesion may not be evident during the early course of the illness and may only appear some months later when fibrosis produces an increasing shortening or deformity of the cusp.

4. *Aneurysm of the sinus of valsalva.* Aneurysms of this area may produce leakage by distortion of the leaflets or by the more acute proc-

ess in which rupture of the aneurysm occurs either into the right auricle or the right ventricle.

5. *Congenital lesions.* These are of several types. The most common is the bicuspid aortic valve which may be complicated either by rheumatic valvulitis or by endocarditis. This lesion is also commonly associated with coarctation. Another form of congenital aortic insufficiency is that associated with fenestration of the valve leaflet. A common variant of this lesion is seen as a single large opening in one cusp. This usually occurs in the most inferior portion of the cusp near its attachment to the aortic ring. This unattached portion of the leaflet is flail and permits large volumes of blood to regurgitate.

6. *Dissecting aneurysm.* Dissection arising in the region of the sinus of Valsalva takes variable forms, ranging from the small intimal tears which communicate with the secondary channel to complete separation of the inner aortic layers from the media at the level just below or just above the coronary orifices. If the patient survives the immediate period following the origin of the aneurysm or if re-entry occurs distally, the picture is that of acute or chronic aortic insufficiency.

7. *Luetic.* This lesion exists in several forms. Aortitis of the ascending root associated with dilation of the valve ring is one of the most readily recognizable forms of this lesion. In other instances the process primarily involves the valve leaflets without major dilation of the aortic root. In these cases one or more valves is densely fibrotic and narrowed with separation of the commissures. Coronary orifices may be markedly affected in this type.

8. *Rheumatoid.* Anatomically this lesion tends to be similar to that which is seen in rheumatic disease.

9. *Rheumatic.* The pathologic picture in this type of disease is highly variable. It ranges from the relatively characteristic picture seen in the patient with aortic insufficiency unassociated with aortic stenosis in which the valve leaflets are relatively little affected, and show only slight to moderate thickening, but in whom the aortic ring is

* This study was supported in part by a grant-in-aid from the National Heart Institute of the National Institutes of Health of the United States Public Health Service.

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considerably dilated. In other instances the valve may be uncalcified but show some fusion of the commissures and a thickening of the cusps which produces shortening. In these there is a central aperture between the leaflets produced by shortening of one or more of the cusps. In still other cases there is calcification of one or more leaflets and associated aortic stenosis. This latter situation presents the most difficult in terms of direct corrective procedures because of the loss of mobility of the leaflets as well as loss of leaflet substance.

With the recognition of the anatomic lesions which produce aortic insufficiency and the development of technical methods which have permitted open visual access to the aortic valve area, it has become feasible to develop the direct methods for the correction of these specific problems. The early approaches to the aortic valve were made under hypothermia alone, but as more complicated procedures were envisioned the time which was required for the procedures has considerably increased. It was necessary therefore to employ extracorporeal cardiopulmonary bypass in conjunction with hypothermia, coronary perfusion, cardioplegia or a combination of the latter. Although some of the procedures which we have employed have been possible without the use of these additional measures, we have come to believe that direct inspection of the valve offers great advantages and that in the complicated or unusual situation closed methods have offered considerable difficulty. The use of potassium citrate and acetylcholine for the production of cardioplegia has offered certain problems in resuscitation of the heart in patients with extreme ventricular enlargement or conduction defects. Restoration of the cardiac beat appears to be more satisfactory following the latter agent than when potassium citrate is used. Incompetence of the aortic valve requires larger amounts of the cardioplegic agent than when the valve is competent because of the loss of material into the large ventricle.

Differential cardiac cooling and induced cardiac arrest by cold alone appear to offer major advantages in patients with advanced disease. With the patient on bypass, cardioplegia can be obtained very rapidly by coronary perfusion at 4 to 6°C. Restoration of cardiac action is rapidly accomplished by the re-establishment of coronary perfusion with blood at normal temperature.

In all operations on the aortic valve by open aortotomy care must be taken to evacuate all air from the left ventricle. Drainage of the left heart is accomplished by the introduction of a catheter through the left atrium just posterior to the interatrial septum. The left heart is allowed to fill and the mitral valve is manipulated to assure that no air is trapped beneath it, before closing of the aortotomy. During the period of arrest it is helpful to irrigate the myocardium with cold saline. Using these general methods a direct approach to the aortic valve is feasible.

The aortotomy itself is made either anteriorly or laterally in the majority of instances. It is preferable to reinforce the aortic suture line with moderately compressed Ivalon, Teflon felt, or tightly knitted Teflon fabric.

Certain of the lesions of the aortic valve can be repaired by suture methods. These include excision of aneurysm of the sinus of Valsalva unruptured or with rupture into the right heart. Acute laceration of a cusp accomplished by direct suture repair or by the additional utilization of reinforcing materials such as Ivalon or pericardium. Endocarditis with destruction of a cusp may occur with involvement of the cusp alone or in combination with perforation into the auricle or ventricle. Visualization of the two openings is essential to complete repair in the combined lesions. Approximation of the aortic wall may be accomplished through the auricle but closure of the cusp should be done from above. Aneurysms of the sinus of Valsalva with rupture can also be repaired by closure of the opening in the base of the cusp utilizing a small plug of material by a closed route or under direct vision.

The majority of the lesions of the aortic valve, however, require reduction in the size of the annulus, addition of substance to a cusp, replacement of an entire cusp, or total valve substitution. The methods which have been devised for the correction of these particular situations must be variable.

Attempts have been made to reduce the diameter of the annulus utilizing a circumferential suture or band which has been tightened to a proper degree to allow approximation of the leaflets.^{1, 6} This procedure has not been entirely satisfactory.

It has been our experience that reduction in the area of the annulus can be obtained more satisfactorily by plication techniques.^{2, 5} Since

1956, extensive studies have been made in cadavers and animals to delineate the possibilities of plication or excision of segments of the aorta in the area of the noncoronary cusp to reduce the total diameter of the aortic root in the region of the valve insertion. These studies demonstrated that the noncoronary cusp can be accurately delineated from outside the aorta if the aortic root is dissected free from the vena cava, right auricle and the pulmonary artery. When this dissection has been accomplished it is possible to clearly outline the commissures of the valve. The origin of the right coronary artery is frequently only a short distance to the left of the anterior commissure of the noncoronary cusp. With temporary inflow occlusion it is possible to place a clamp which includes only the aortic wall of the noncoronary cusp. This maneuver may be used to reduce the distance between the two commissures of this leaflet or to bring together completely the commissures of the remaining two cusps to form a bicuspid valve. By inserting a finger in the aorta the valve cusp can be brought into the clamp for excision. If pressures in the femoral arteries are monitored and the insufficiency is

well controlled, there is an immediate rise in the diastolic pressure to normal levels. Sutures may then be placed in the aortic root at this area and the excess aortic wall removed. This indirect procedure, while associated with considerable technical difficulty, has been satisfactory in restoring normal dynamics and in eliminating the leakage when simple annular dilation has been the cause of the insufficiency. If sutures are not taken directly through the commissural zones but are permitted to emerge through the lower portion of the thin walled aorta, the high pressure in this area can result in cutting through of sutures in the lower aspect of the sinus of Valsalva. Serious hemorrhage can result unless these sutures are reinforced with small patches of a buttressing material (fig. 1).

Although the closed technique had certain inherent advantages, the lack of visualization of the valve orifice and the inability to correct all situations by this method led to the development of other methods for the reconstruction of the aortic valve. Under conditions of extracorporeal bypass and open aortotomy it is possible to accomplish a similar plication under direct vision.

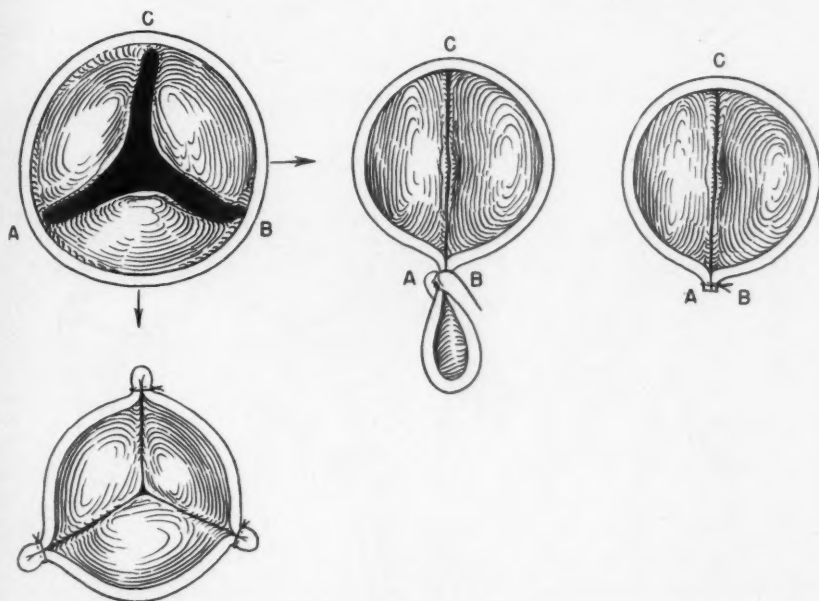


FIG. 1. Patulous aortic valve with well preserved cusps. Methods of correction are shown. Conversion to a bicuspid valve by removal of the noncoronary sinus is shown to the left. Narrowing of the annulus by plication with mattress sutures at the commissures is shown below.

This has been more satisfactory in that the competency of the valve can be ascertained by vision. In such instances it is also possible to excise the leaflet of the noncoronary cusp and to convert the valve into competent bicuspid valves, as shown by Garmella and associates⁴ and in our laboratory.⁵ Since the aortic annulus is already greatly dilated in the majority of these instances, the excision of this one-third of the circumference has not reduced the aortic diameter to the degree which produces obstruction. Indeed, in the majority of cases the aortic annulus then approximates its usual area.

Still other situations exist in which the cusps are separated from each other or at one or more commissures. To reduce the circumference of the annulus at one or more points, mattress sutures can be used to bring the leaflets together, leaving a tricuspid valve. This method has its particular application in luetic disease of certain types.

Some forms of aortic insufficiency show rather marked stiffening of one or more leaflets and curling of such leaflets. If this deformity is not excessive it is possible to close the gap which is left by the shortened leaflet or leaflets by the

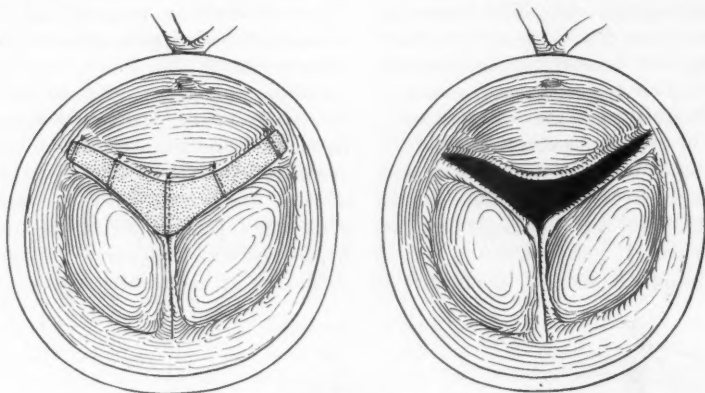


FIG. 2. Illustration showing the addition of substance to a scarred leaflet

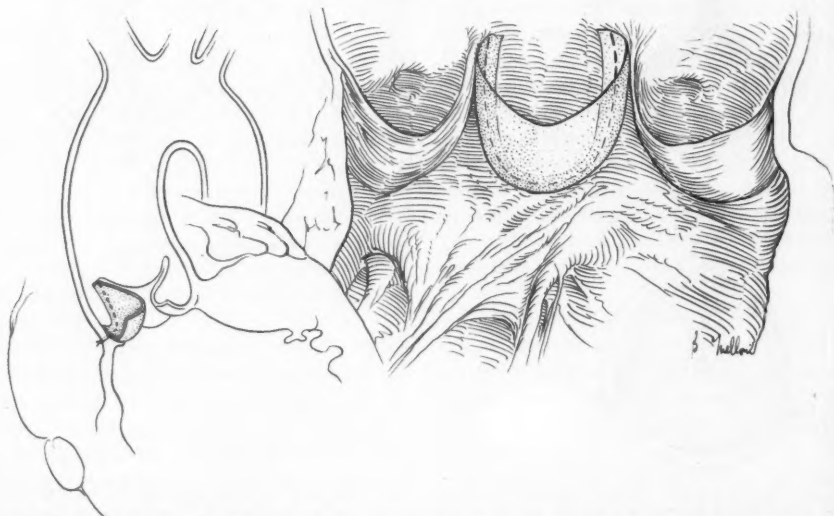


FIG. 3. A "self-sealing" artificial cusp sutured in the position of the excised aortic cusp

addition of a small amount of additional substance sutured to the edge of the leaflet. Pledgets of Ivalon have been utilized for this purpose, held in place by interrupted sutures to the leaflets as shown in figure 2. Similar additions to the cusp can be made to restore its ability to coapt, using Dacron or Teflon cloth providing these are anchored to the leaflet and to the commissures as well.

The destruction or loss of one cusp was recognized early in the investigation of this problem. Endocarditis, rheumatic disease or a combination of both are particularly prone to this lesion. Single cusps have therefore been developed which reproduce essentially the essential architecture of the normal leaflet. Leaflets themselves have been constructed of silastic and other plastic materials. To date, the physical characteristics of the silastic material appear to be the most desirable. The design of the leaflet has been gradually altered

to evolve what we have termed a "self-sealing leaflet." A small flap of material is molded to conform to the contour of the aortic wall at the edge of the artificial leaflet. When blood fills the cusp in diastole this flap follows the movement of the aortic root to provide additional sealing. This thin edge left beyond the suture line in contact with the aortic wall closes any small openings which may be left between the sutures until healing can occur. This would appear to be an important addition to the stability of the placement of the leaflet. Placing sutures through the prosthesis at the upper end of the commissure is quite satisfactory in most areas. Great care should be taken not to place sutures in the region of the auriculoventricular node when an entire cusp is being placed into the left posterior sinus. Further experimental development of this single leaflet replacement is the incorporation of small pins into the base of the leaflet. These are of suffi-

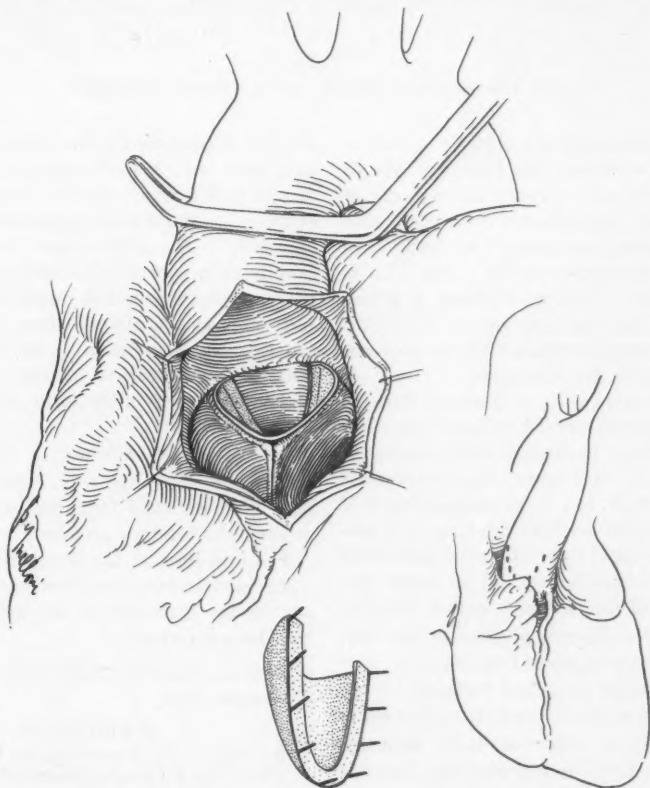


FIG. 4. An artificial aortic leaflet with pin type fixation incorporated into the periphery

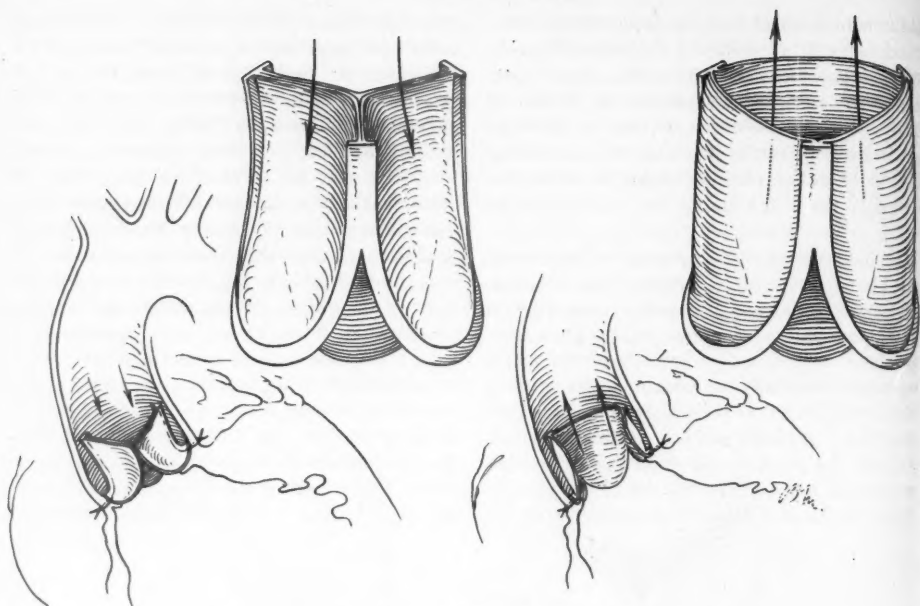


FIG. 5. Tricuspid "self-sealing" aortic valvular prosthesis

cient length to penetrate the aortic wall following which they are bent in the form of staples to hold the leaflet in place without the necessity of suture. The slight angulation of these points aids in fixation in those areas in which the leaflet does not come to the exterior of the aorta. This is shown in figures 3 and 4. Utilizing a suture method, more than one cusp can be replaced if necessary. Attempts to replace all three cusps are now being made in the laboratory.

Experimental total valve replacement has also been made in several ways. A tricuspid valve has been devised which incorporates the features of the cusp with all three cusps being mounted as a single unit (fig. 5). If a small margin of each of the diseased leaflets is left at the base, it is possible to fix a tricuspid valve at a point just above the remaining commissures and to utilize the lower portions of the old valve leaflets for seating. Suture of the superior portions of the commissures then gives excellent fixation.

The development of several methods for the direct correction of aortic insufficiency has led to greater certainty of correction in the approach to this lesion. These incorporate the desirable

features of correction of the leak at the subcoronary level with the advantages of mobilization of such leaflets which may be impaired by fusion of the commissural zones. Utilization of the direct approach to the aortic valve also permits the simultaneous correction of lesions of the mitral valve, particularly mitral insufficiency under direct vision at a single procedure. Refinements in the technical application of the principles here outlined enable one to correct, essentially, all regurgitant lesions of the aortic valve in a definitive approach.

SUMMARY

The pathologic types of aortic insufficiency have been reviewed from the viewpoint of the anatomic lesions they produce.

The principles of the direct approach to the aortic valve have been outlined and specific methods for the correction of the individual lesions have been described.

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ELECTRICAL BURNS OF THE LIPS: A MODIFIED PLAN OF TREATMENT

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The problem arising from electrical burns of the lips and mouth has been reported by Schultz¹ and more recently by Kazanjian.² My experiences during the past 3 years at this institution corrob-

are identical with other electrical burns in that they are well localized but usually quite deep, extending through the entire thickness of the lip. In 3 cases there was associated injury of the

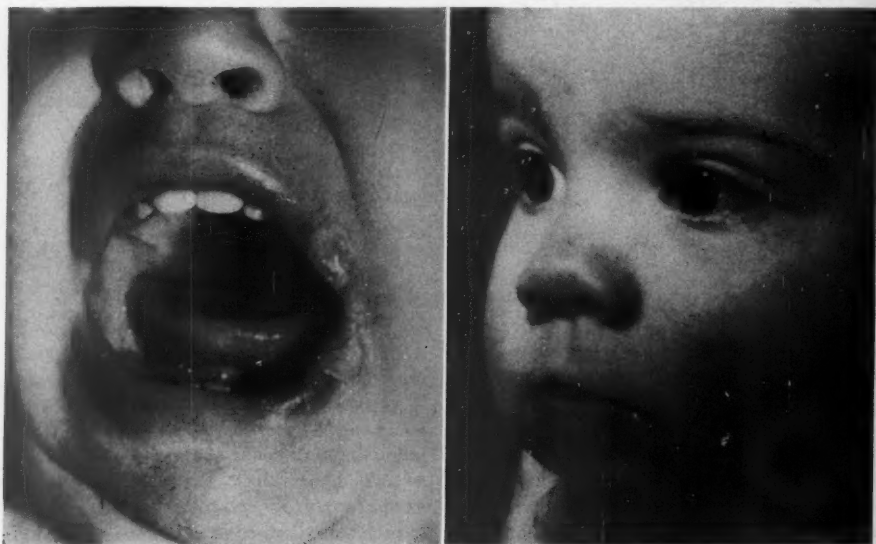


FIG. 1. A third degree burn of limited size corrected by excision and primary closure.

rate their findings regarding the mechanism and types of injury incurred. Infants and very young children are most affected and the lower lip and angle of the mouth the most frequent site. In all of the 5 cases seen here during this period, the burns resulted from sucking on the end of an extension cord. The saline content of the saliva acted as an electrolyte and completed the electrical circuit causing an electrical burn of the arc rather than the contact type as differentiated by Baldrige.¹ In none of these cases did the burn result from chewing through the insulation of the wire although this has been reported elsewhere.³

The pathologic characteristics of these burns

tongue, but in none of these did this constitute any significant problem. There was no evidence of burn shock. That their similarity corresponds to electrical burns in general is evidenced by the immediate and complete electrocoagulation of the involved tissue, resulting in complete isolation of the burned area from the systemic circulation. It is also interesting that these injuries were practically painless.

Previous reports on this condition have recommended early debridement and encouragement of spontaneous epithelization with later definitive plastic repair.^{1, 2} In 4 of the 5 cases treated here a different course of management was employed. This consisted of early excision of the burn with primary closure of the resulting defect. By achieving primary healing, this approach to the prob-

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lem minimizes morbidity and scarring, thus making secondary operations easier and, in the less severe injuries, totally unnecessary (fig. 1). Success in this surgical approach depends primarily on three factors.

The first of these is the proper timing of the operative procedure. Sufficient time must elapse to permit accurate and definite demarcation of the nonviable tissue, and thus ensure its complete extirpation without sacrifice of adjacent vi-

able tissue. At the same time undue delay is dangerous if secondary infection is to be avoided. Surgical intervention between the 4th and 7th days seems to satisfy both of these requirements.

The second factor involves control of infection, which is accomplished by early institution of antibiotic therapy. The orally administered wide spectrum antibiotics which include an antifungal agent have been employed in these cases.

The third factor to be considered is the tech-

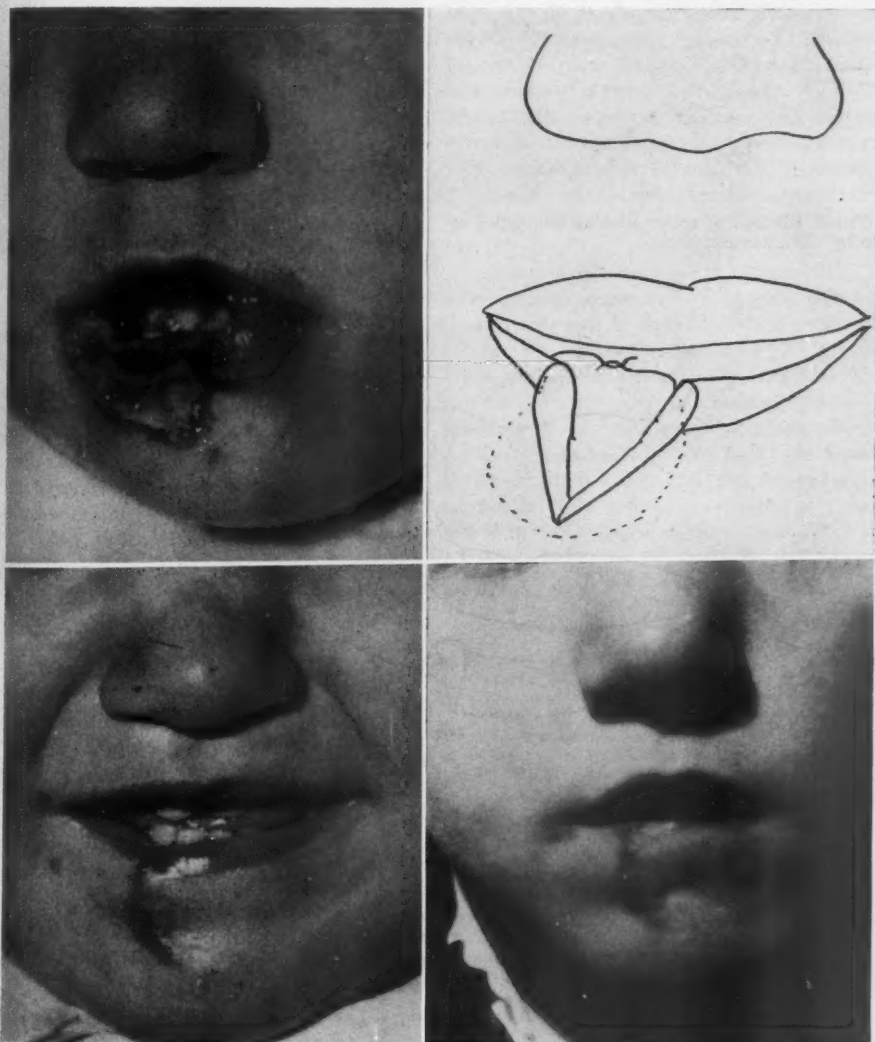


FIG. 2. A more extensive burn of lower lip corrected by one stage excision and primary wire closure. Immediate and late result show adequate lip growth. Revision of scar is planned.

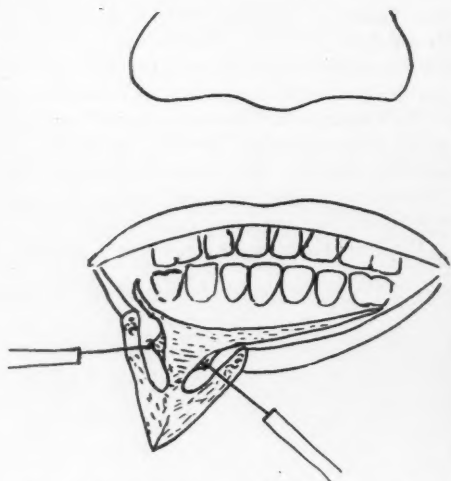


FIG. 3. Method of accomplishing mucosal closure by advancement flaps.



FIG. 4. Extensive burn at angle of mouth

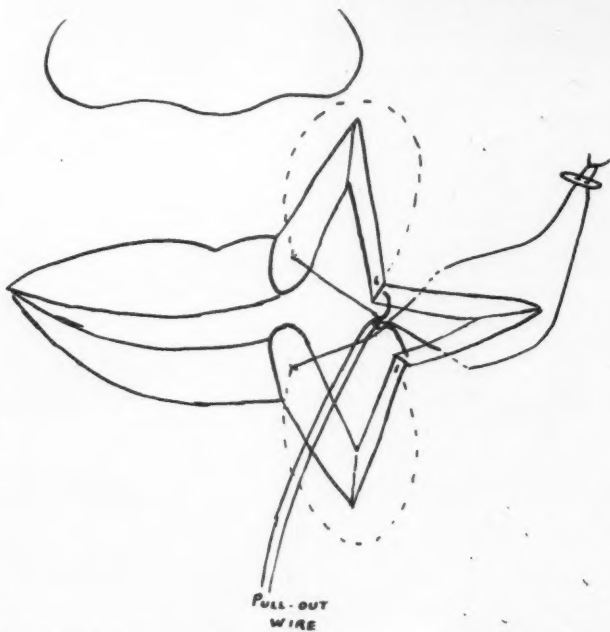


FIG. 5. Method of closure with no. 34 gauge stainless steel wire. The pull out wire is brought out through the line of closure.



FIG. 6. Immediate result—further revision with correction of microstomia of left angle of mouth will be carried out at a later date.

nique employed in closure of the defect in the lip. This must be individualized to meet the specific problem at hand. Usually some type of holding suture is required owing to the tension under which the larger defects must be closed. Through-and-through sutures across the line of closure are to be avoided because of the disfiguring scars that often result. These are still seen occasionally on the older, poorly closed cleft lips. The type of suture which has proved useful in closure of the wide "V"-shaped defect is a circular intramuscular suture of No. 32 or No. 34 gauge stainless steel wire which is tied within the closure line of the vermilion of the lip (fig. 2). It is left in place for approximately 2 weeks. The skin edges are approximated with 5-0 or 6-0 nylon suture. Closure of the mucosal surface often requires advancement of a flap of adjacent gingivobuccal

mucosa. This is readily accomplished by an incision in this sulcus on each side of the defect in the same manner in which the mucosal closure is accomplished in the cleft lip repair (fig. 3). Although closure of some of the wider defects leaves a tight lip, improvement can be expected in the growing child. Therefore lip switch procedures of the Abbe-Stein-Estlander type have not been employed as primary procedures but would be feasible in older individuals.

Burns at the angle of the mouth are slightly more difficult to manage. Closure in such a burn (fig. 4) was achieved by conversion of the defect into three triangular areas with approximation of all angles at a point as far laterally as possible. The subcutaneous wire tension suture was tied over a button and a pull-out wire was incorporated to facilitate its removal (fig. 5). Satisfactory healing was obtained, but secondary revision will obviously be required when the child is older (fig. 6).

It is our conclusion from these cases that primary excision of electrical burns of the lips with immediate repair is feasible if supplemented by the use of adequate antibiotic therapy. This provides obvious advantages over methods which depend upon slow secondary healing. It does not appear to involve any appreciable surgical risk. Adequate anesthesia is achieved by local block of the infraorbital and/or mental nerves supplemented by light general anesthesia, thus minimizing the possibility of anesthetic complications.

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THE RELATIONSHIP OF TRAUMA TO ARTHRITIS*

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Since the majority of individuals who have some type of arthritis are able to pursue a gainful occupation and participate in the average activities of everyday living, it can be readily seen that a percentage of these will be subjected to trauma of some type. The number of people who have arthritis is not known. In many the symptoms are minor or absent. The estimate of individuals who have some type of arthritis and "rheumatism" is staggering. It has been estimated that approximately 25 million persons in this country have some degree of osteoarthritis or degenerative arthritis.^{1,5}

From the compensation viewpoint the relationship of injury to the disability of the working man is ever assuming an increasing importance. The physician must be aware of any anatomic and physiologic conditions that might be factors in the production of the disability. Because of the widespread incidence of arthritis among the population, the relationship of trauma to arthritis must be ever present in the evaluation of these cases. There may be x-ray evidence of arthritis present for a long time without clinical signs or symptoms.

According to Doub,⁷ the words "traumatic arthritis" are interpreted as those chronic changes in and around the joint after injury, that resemble or simulate the arthritis commonly classified as hypertrophic, degenerative, osteoarthritis and arthritis deformans. For practical purposes, and from an underlying basic pathologic aspect, traumatic arthritis and osteoarthritis may be used interchangeably.

The following aspects of the relationship of trauma to arthritis are significant from the medical and legal point of view: (1) Are certain types of arthritis the result of trauma? If so, what type of injury, or how severe is an injury to bring about such changes? The time factor between injury and joint changes is of prime consideration. (2) The relationship between trauma to a known, existing arthritic.

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The extent to which arthritic changes may well be present with minimal or no symptoms, but activated by trauma, is frequently seen in the case of the sprains of the cervical spine in which x-rays taken immediately after the accident will show extensive pre-existing degenerative changes in the cervical spine. For such changes to result directly from trauma would require many months or years. Rehabilitation is delayed and prolonged in persons with arthritis. Trauma seems to be a "trigger mechanism" in activating arthritis.

In order that the physician, insurance adjusters, and the legal counsellors involved may have a clearer understanding of the underlying changes which occur in the various types of arthritis, the following discussion and illustrations are included. Osteophytosis is due to the degenerative changes which occur in the intervertebral spaces with resulting bridging between the vertebral bodies, resulting in a "loss of normal elasticity" of the ligaments. With the progress of the degenerative changes there occurs a concomitant degeneration in the articular facets, the small joints of the spine, wherein degenerative osteoarthritic changes do develop. From the illustrations it can be seen that joints involved by arthritis would most likely not respond to trauma as would a normal joint.

The anatomy of the normal joint may be discussed briefly. A typical diarthrodial joint is a freely movable joint lined with synovial membrane.⁴ The bones making up such a joint are cancellous in nature, having a thin cortical layer and a subchondral plate on which is the articular cartilage.³ The movable portion of the joint is covered with articular hyaline cartilage which in its normal state is smooth and glistening (fig. 1). There is a variation from the normal in the various types of arthritis discussed below.

RHEUMATOID ARTHRITIS

Early stage. (1) Initial changes in synovia: hyperemia, edema, increased joint fluid hyperplasia and focal collections of small round cells (usually lymphocytes and plasma cells); (2) beginning pannus formation: hyperplastic over-

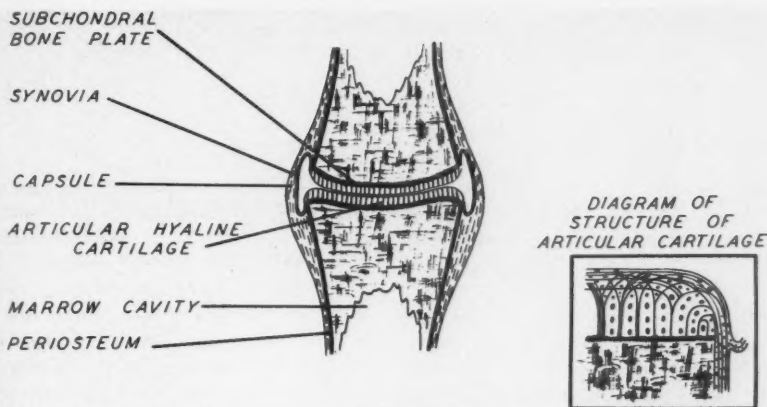


Fig. 1. Diagram of mechanical conformation of a normal joint. Note subchondral bone plate

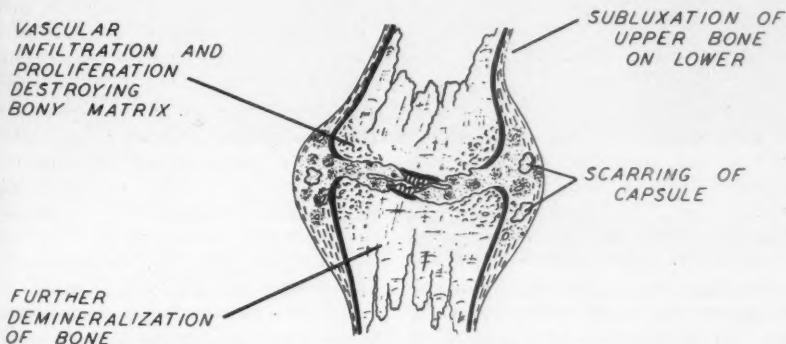


Fig. 2. Diagram of advanced rheumatoid arthritis with bony ankylosis. The joint space is obliterated and there is continuity of trabecular patterns across the joint line. In very late stages, there is reossification of the adjacent bony matrix.

growths of synovia at its junction with articular cartilage (spreads like a carpet over cartilage from periphery to center) varies from avascular granulation tissue to an avascular fibrous tissue; (3) subchondral bone changes (replaced by granulation tissue): osteoclastic activity beneath cartilage perforates the lamellar plate and permits access of granulation tissue to articular cartilage; (4) early osteoporosis; (5) symptomatic (fig. 2).¹⁶

Moderately advanced stage. (1) Increased pannus formation; (2) chondroclastic activity with cartilage destruction, most advanced at periphery; (3) progression of subchondral marrow fibrosis; (4) increased villi formation with rice bodies which may be free in joint; (5) fibrous ankylosis may be seen in this stage; (6) subcutaneous

nodules and associated tissue changes in liver, spleen, muscle, nerves, pericardium and pleura.

Advanced stage. (1) Increasing cartilage destruction and fibrous ankylosis (union of pannus on opposed surfaces to obliterate the joint); (2) fibrous ankylosis may progress to bony ankylosis, with bone striations crossing the joint line; (3) with bone ankylosis, reossification of adjacent bone usually begins; (4) bony erosion, near articular margins, cystic in nature, filled with granulation tissue; (5) subluxation.¹⁷

Roentgenographic changes. (1) Soft tissues (periarticular edema); (2) regional bones: progressive deossification with depletion of metaphyseal reserve sites, thinning of cortex, coarsening of trabecular pattern; possibly subarticular cortical cystic dissolutions (very late reossification); (3)

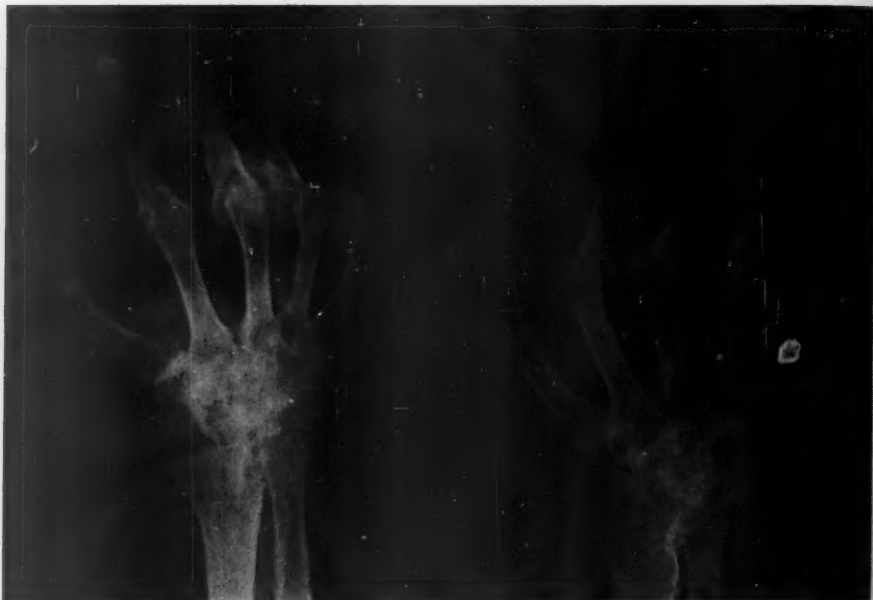


FIG. 3. Advanced rheumatoid arthritic deformities of the wrist and fingers. Subluxation of the metacarpophalangeal joints.

articular cortex (thin); contours irregular but surfaces smooth; (4) joint space: reduced, interosseous spacing possibly obliterated by ankylosis; (fibrous in type, until very late—bony ankylosis); (5) irregularities in alignment of bones: actual subluxations, ulnar, deviations of fingers and so forth (fig. 3).

ANKYLOSING SPONDYLITIS

(1) Multiple arthritis with ankylosis of posterior intervertebral joints (apophyseal or facets), costovertebral, sacroiliac, ossification of spinal ligaments and margins of intervertebral discs; (2) *synonyms*: (a) spondylarthritis ankylopoietica, (b) Marie-Strümpell disease, (c) spondylose rhizomelique, (d) Bechterew's disease, (e) spondylitis ossificans ligamentosa, and (f) adolescent spondylitis; (3) probably a spinal form of rheumatoid arthritis; (4) osteoporosis of the vertebrae; (5) *intervertebral discs*: this condition does not originate in nucleus pulposus. There is ossification in outer fibers of annulus fibrosus giving roentgenographic picture of the bamboo spine. New bone enters the epiphyseal ring of vertebral body on either side, eventually meets and joins about middle of disc. (6) Ossification occurs early

in capsule and capsular ligaments of posterior intervertebral joints and costovertebral joints. This process precedes bony union of vertebral bodies. (7) *End stage*: fusion of all vertebrae, one to another by ossification across posterior apophyseal joints and across intervertebral discs, ribs to vertebrae by ossification across costovertebral and costotransverse joints, ankylosis of sacroiliac joints, often the hips and the sternoclavicular joints. Any or all ligaments of the spine may become ossified, including longitudinal ligaments and ligamenta flava.

The cervical spine shown in figure 4 illustrates the roentgenographic changes in this type of arthritis. Osteoporosis of the vertebrae is clearly seen in the clinical roentgenogram. There is usually a loss of the normal cervical lordosis. The pathologic process may involve primarily the posterior structures (the interspinous and the interlaminar ligaments and the articular facets) before there is ossification in the peripheral fibers of the annulus fibrosus. The disease may and usually does involve the entire spine. In the clinical roentgenogram of this region of the spine there is a loss of the normal lumbar lordosis and the patient develops "poker back" (fig. 5).



FIG. 4. Advanced rheumatoid spondylitis of the cervical spine. Loss of normal cervical lordosis and all mobility. Such a spine lacks the flexibility and resiliency of a normal spine.



FIG. 5. Bamboo spine of rheumatoid spondylitis. End result of a "burned out spondylitis."

OSTEOARTHRITIS

Early stage. (1) Initial changes in superficial articular cartilage, from wet, smooth, glistening and white to dry, dull and yellowish; (2) fissure formation, flaking and fibrillation (degeneration of hyaline matrix with resultant loss of binding substance between collagenous fiber bundles); (3) early subchondral sclerosis and condensation; (4) increased density of bone at weightbearing areas; (5) proliferation of fibrocartilage from tissue walls; may be extruded to form a "loose body"; (6) no marginal hyperplasia at this time; (7) no capsular changes; (8) usually asymptomatic (fig. 6).

Moderately advanced stage. (1) Cartilage becomes thinner at points of weightbearing and where friction is greatest; (2) marginal hyperplasia and osteophytes begin to appear at junction of perichondrium and periosteum; (3) beginning capsular changes, hyperplasia with villi and folds; (4) osteochondromas form in capsule and may be

replaced in bone; (5) osteophytes form in cartilage and may be transformed to cancellous bone; (6) early alterations in contour of articular cartilage and molding of bone ends; (7) usually symptomatic.

Advanced stage. (1) Complete loss of cartilage with eburnation of exposed bone. The cortex becomes smooth and polished, often grooved; (2) progressive marginal hyperplasia and enlargement of marginal osteophytes which may become exostoses, cancellous bone of which is continuous with marrow or major bone involved; (3) progressive changes in capsule with loose body formation, fractured marginal exostoses or detached synovial chondromas or osteochondroma; (4) subchondral cysts containing mucoid material in areas of sclerosis, subchondral minute fractures; (5) progressive changes in contour of joint; (6) symptomatic. Symptoms vary with extent of changes and joint involved (fig. 7).

Roentgenographic changes. (1) *Early stage:* usu-

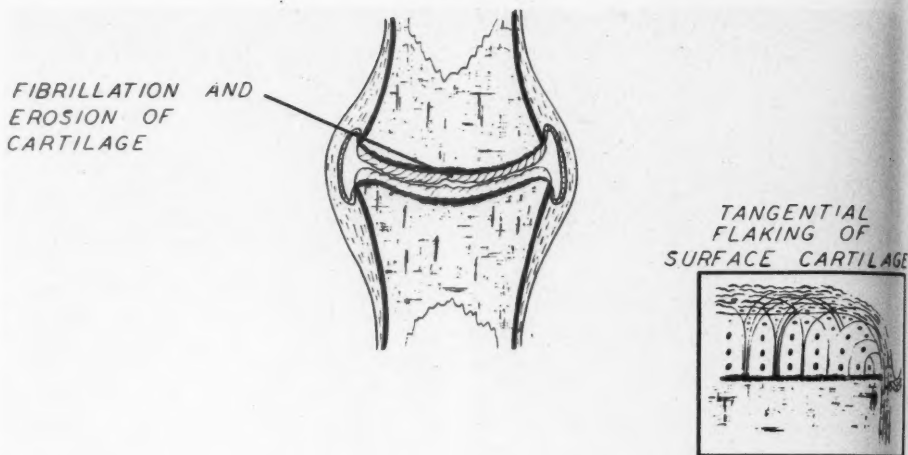


FIG. 6. Diagram showing fibrillation and erosion of cartilage in early osteoarthritis

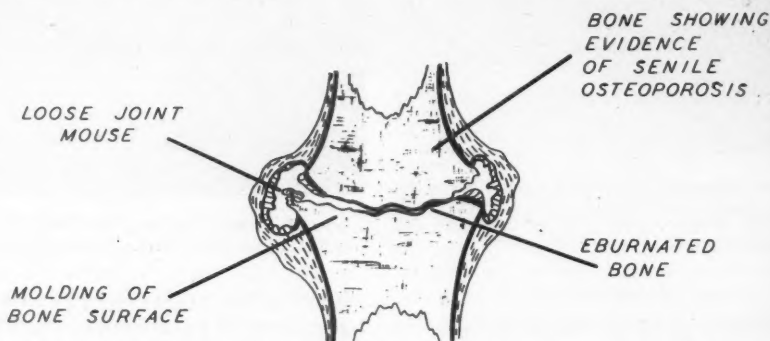


FIG. 7. Far advanced osteoarthritis. Ankylosis does not occur as in rheumatoid arthritis. Note "mechanical moulding" of adjacent bone surfaces.

ally negative since changes are limited to superficial layers of articular cartilage; (2) *moderately advanced*: (a) narrowed joint space, (b) beginning marginal osteophytic formation, and (c) beginning increased density in subchondral bone at site of greatest pressure; (3) *advanced*: (a) progressive narrowing of joint, (b) increased marginal osteophytic formation, and (c) osteochondromas may appear in capsule.

Eburnation, the result of erosion and wearing away of the articular cartilage with resultant polishing of the subchondral bone, is a common finding in osteoarthritis (fig. 8). Marginal hyperplasia, roughening of the articular surface and subchondral cystic changes are also frequent findings of osteoarthritis.

OSTEOPHYTOSIS

(1) Usually multiple, occasionally single, on one side of vertebral column; (2) frequently incidental findings of routine roentgenographs; (3) may cause no symptoms; (4) lie anterolateral and not true anteriorly; (5) may or may not be joined together; (6) space between two "kissing" osteophytes usually contains disc material; (7) due to degeneration and "flowing" anterior of the disc material; (8) often confused with true osteoarthritis (latter can occur only in apophyseal joints or facets which are true diarthrodial joints containing synovial membrane. The intervertebral "joint" is a secondary "cartilaginous joint"); (9) *synonyms*: (a) spondylitis osteoarthritis



FIG. 8. Anterior photograph of the distal end of a left humerus. Example of wearing away of articular cartilage and "polishing or eburnation" of underlying subchondral bone plate.

(Knaggs), (b) polyspondylitis marginalis osteophytica (Shore), (c) spondylitis deformans (Ben-
ecke), and (d) spondylosis deformans (Smorl);
(10) forward protrusion of disc is prevented by
firm anterior ligament; (11) consists of new periosteal bone; (12) rarely forms on posterior surface
because collapsed disc compresses anteriorly; (13)
usually associated with narrowing of interverte-
bral space; (14) no evidence to show that this is
osteoarthritis, except that both occur in later
years of life; (15) osteoarthritis is not necessary
to formation of osteophytes of vertebrae.

The upper part of the spine shown in figure 9
clearly illustrates osteophytosis. It can be seen
that grossly the articular facet is uninvolved.
This condition is often encountered in routine
roentgenograms taken for other reasons. They
usually cause little or no symptoms *per se*. The
protuberances consist of new periosteal bone and
rarely form on the posterior surfaces because the
intervertebral disc material is compressed an-
teriorly. It may be said that the intervertebral
space is not a true joint from the anatomic view-
point. It is a secondary "cartilaginous joint" and
not a diarthrodial joint containing synovial mem-
brane. It is believed that disc degeneration is the
most likely etiologic factor in the formation of



FIG. 9. Lateral view of dorsal spine with osteo-
phytosis, or spondylophytosis. Note osteophytic
outgrowths between upper two vertebrae. Results
from intervertebral disc degeneration.

osteophytes. As the disc material flows anteriorly, the periosteum is elevated and new bone is laid down.

DISCUSSION

In regard to rheumatoid arthritis, again the problem arises as to what extent, if any, injury may have aggravated the pre-existing rheumatoid arthritic status. Injury to a well established rheumatoid arthritic joint may well cause symptoms for a period of from 2 to 6 months. A problem occasionally arises wherein trauma to an individual joint heretofore considered normal later manifests rheumatoid arthritic changes. The question in this situation is: "Did the injury cause the rheumatoid arthritis?" It is the consensus of opinion that trauma is not a significant etiological factor in the development of rheumatoid arthritis, which is, in the light of present knowledge, a constitutional condition.

Jonsson and Berglund¹⁰ reported that between 1936 and 1948, 2236 cases of rheumatoid arthritis were treated, of which 12 patients gave a definite history of trauma. It was felt, however, that in general, trauma should be disregarded as an etiological agent of rheumatoid arthritis. However, in some cases, it may be difficult to completely eliminate the factor of trauma in the development of rheumatoid arthritis.

Although a patient with a rheumatoid spondylitis is not likely to be engaged in heavy manual labor which would come under the compensation aspect, he might be involved in a liability situation and the question here, again, is: "Did the injury aggravate the pre-existing rheumatoid spondylitis?" It is felt that an injury to such a back may well aggravate symptoms over a period of many months.

Stamm¹⁵ believed that osteoarthritis develops in a normal joint as a result of trauma, and feels that the significant factor is one of a mechanical process.

Any fracture near to or into the articular surface of a joint may result in osteoarthritic degenerative changes developing within the joint. Even though the fracture may not involve the joint, but be adjacent to it, the result in some degree, however little, of a malunion, the resulting malalignment of the corresponding surfaces constituting the joint, is conducive to developing osteoarthritic changes. A fracture of the proximal end of the tibia, although united, but in a malposition, resulting in a knock-knee or bowleg

deformity, might well constitute the mechanical basis for a subsequent development of degenerative changes in the knee.

Fractures of the patella, even though repaired by open reduction and internal fixation, may well result in a roughening of the undersurface of the patella and be a significant factor in the development of an osteoarthritis of the knee. At times a patellectomy is preferable to an attempted repair of the fractured patella because of the inability to bring about a smooth alignment of the undersurface of the patella.

The "dashboard" type of injury which presents the usual clinical picture of a posterior dislocation of the hip associated with a fracture of the acetabulum, may well result in a latent type of degenerative arthritis.

Fractures of the os calcis with an interruption of the subastragalar joint, a significant weight-bearing joint, are often associated with latent osteoarthritic changes.

Williams and Lockie¹⁸ mentioned that when trauma occurs to a joint, which has been established by x-ray or otherwise as normal, any disability resulting from an injury to the joint must be assumed to be the result of the injury. They also inferred that an injury which may be disabling to a particular type of worker may be less disabling to one who does not have to use the particular part of the body. They define disability as "an impairment of the ability to work or to use a part of the body."

It is felt that aggravation of pre-existing osteoarthritis may continue from one week to several years. A formula whereby the extent of the aggravation of the pre-existing arthritis could be established would be highly desirable. There is little doubt but that trauma will aggravate symptomatically an osteoarthritis existing in peripheral joints as well as in the spine. It is to be expected that few individuals who suffer back injuries will admit having had any distress or disability before the accident. A patient with a pre-existing osteoarthritis who is involved in a relatively trivial accident may well complain of symptoms out of proportion to the objective findings. It is admitted that the spine presents quite a problem from the viewpoint of an assessment of the evaluation of the aggravation of a pre-existing osteoarthritis. Of all the portions of the body the back is the most likely anatomical region wherein lies the greatest challenge to the

physician in the assessment of disability. A workman, injuring his back by simply leaning forward and picking up a heavy object, may complain for months of his back, basing his complaints on the individual single incident, and denying that he had any previous difficulty with his back. The necessity of recording in detail the clinical history cannot be overemphasized.

If some objective, tangible method could be developed whereby the extent of aggravation of a pre-existing arthritic condition could be on a tabular basis, then the entire situation might well assume a more equitable viewpoint.

Sonntag¹⁴ believed that arthritis could occur as early as 4 weeks after an injury, or it may be delayed over a period of many years. As a rule, it requires about 6 months after injury for clinical and roentgenologic signs to develop. The more severe the initial injury, the earlier changes will develop in the joint.

As stated previously, in general the changes which develop in traumatic arthritis are comparable to those in hypertrophic arthritis. Hypertrophic arthritis is likely to be generalized, and is a normal physiologic degenerative process. Traumatic arthritis, on the other hand, is localized to the joint which had been subjected to a definite injury or repeated minor injuries. The extent to which injury can aggravate an already existing arthritis is of particular importance in the evaluation of these cases.

It is a challenge to the physician to differentiate between the acute symptoms which follow any injury to a joint, whether there is arthritis or not, and the more permanent, lasting type of symptoms that would suggest or indicate some pre-existing arthritic changes. Many cases are seen where the acute response to the injury subsides with no lasting disability. It is the consensus of opinion among authors that injury to the cartilage is the principal underlying factor in the development of traumatic arthritis. As mentioned above, it is most difficult to evaluate the time element in the development of changes resulting from injury. The judgment of the physician must be influenced by many factors. If, years after injury, a joint develops arthritic changes it is most likely of a nontraumatic nature. Changes occur in joints as a result of abnormal stresses and strains. The spine, particularly, is subject to degenerative changes in advancing years. This is most likely to be generalized and involve large

segments of the spine. On the other hand, if the changes are localized and there is a definite history of an injury to a particular portion of the spine, the cause or relationship must be carefully evaluated. In cases where x-rays for some reason have been taken before the injury to a joint, the evaluation of the relationship between injury and later joint changes is much more definite.

Doub⁷ concluded that certain criteria must be compiled with and substantiated before the diagnosis of a traumatic arthritis is made. These are: (1) there must be proof of injury and its severity; (2) the injury must have been applied to the joint in question; (3) the status of the joint before injury is important; (4) the time interval between injury and the development of pathologic changes must be within the generally accepted limits; and (5) there must be clinical and roentgenologic evidence of pathologic tissue changes.

It is a known fact that the clinical findings and symptoms are not in direct proportion to the roentgenologic evidence of degenerative changes in a joint. Cases with severe degenerative changes may show slight or minimal symptoms and clinical findings.

The smooth, gliding, well fitting surfaces of a joint are masterpieces of architecture and mechanics. When any condition brings about a change within the joint resulting in irregularities of the joint surfaces, this relationship is disturbed.

With more persons living a longer life, the problem of degenerative or osteoarthritis is ever increasing. Simple trauma such as a sprain to an arthritic joint may well result in disability far out of proportion to the extent of the initial injury. The mechanism of a sprain in an arthritic ankle may cause more disability than a fracture in or near an otherwise normal ankle joint. Fractures into joint surfaces or near joints that cause a malalignment of the joint surfaces are prone to result in progressive degenerative changes within the joint.

Axhausen² believed that the injury must be severe enough to damage the cartilage in order to produce arthritis deformans. He also recognized the fact that patients with this type of arthritis would react to even slight injury.

According to Key,¹¹ the injury to the joint may be of several types: (1) a single, severe injury to the joint cartilage; (2) repeated, mild trauma to the joint cartilage; (3) disorganization of the me-

chanics of the joint; and (4) faulty weightbearing caused by bony deformities so that use brings about repeated injury to the joint surface. An injury to an internal semilunar cartilage, with resulting chronic irritation and minimal trauma to the cartilage of the joint, will bring about hypertrophic arthritis, or traumatic arthritic changes.

Depressed fractures of the tibial plateau will result in inequality of weightbearing of the femoral condyles on the tibial plateau and result in eburnation and sclerosis and degenerative changes of the knee.

Fractures of the head of the radius, although they may remain in good position, will often bring about degenerative changes on the capitulum of the humerus.

It must be remembered that any fracture that extends into a joint line and brings about a dissolution of the continuity of the cartilage may ultimately result in a traumatic type of arthritis. As a rule, the degree of osteo or traumatic arthritis is directly in proportion with the amount of displacement of the fracture, particularly in weightbearing joints.

A convincing example of the result of malalignment of joint surfaces as a causative factor in degenerative arthritis is seen repeatedly in cases of knock-knee, or bowlegs which have begun in childhood, but as time goes on, with the resulting malalignment, there results degenerative changes of the articular surface.

Traumatic arthritis results from any alteration of contour of joint surfaces, such as: (a) hip dysplasia; (b) Legg-Perthe's disease; (c) Freiberg's disease; (d) Köhler's disease; (e) Kienbock's disease; (f) slipped femoral epiphysis; (g) fractures into joint surfaces, as depressed tibial plateau; (h) osteochondritis dissecans, with loose body causing defect in articular surface.

Osteo or degenerative arthritis is a disease of middle age and is seen most frequently among individuals who have performed manual labor, or who have had some static deformities, with resulting unusual strain upon the involved joints. It is rather interesting to note that the degree of degenerative changes as manifested by x-rays does not bear any direct relationship to the degree of clinical symptoms. Degenerative arthritic changes are seen frequently in the spine. Because of the changes that occur in the intervertebral space, osteophytes form around the vertebral margins.

Fisher⁸ believed that where trauma is the direct etiologic factor it is due to frequently repeated traumas, whereas in cases where trauma is the predisposing factor it is most likely to be caused by a solitary injury.

It is a well recognized fact that trauma to joints may result in latent degenerative changes in the joints.¹² This is the type classified as "traumatic arthritis" or osteoarthritis. In discussing the subject of the relationship of trauma to arthritis the difficulty of evaluating the relationship of trauma to the arthritis is apparent. There is always the factor of the physiologic progress of the arthritis with or without trauma. Trauma may aggravate a pre-existing, recognized case of arthritis, or may "activate" an otherwise non-symptomatic, dormant arthritis. The difficulty arises in assessing the relative disability attributed to an injury when arthritis is known, or even not known, but later discovered.

That trauma can aggravate pre-existing arthritis, either of the rheumatoid or osteoarthritic types, is frequently confirmed by the apparent "flare-up" of arthritis in the small finger joints in a person who has had a fracture of the wrist. The surgeon is always aware of this possibility in the treatment of fractures in a known arthritic.

Cotton,⁶ in a discussion on traumatic arthritis, stated: "The debatable questions are: (1) has the injury in any way increased the rate of progress in the joint pathology; or (2) has there been a return to the *status quo*, or some persistence of disability or discomfort, some impairment of recovery irrespective of any increase in the lesions? These questions always will be debatable, case for case, unless there be x-ray evidence previous to, or promptly after, the injury."

Shorbe and Harsa¹³ discussed the magnitude of arthritis from a social and economic viewpoint. They stated that approximately 97 million work-days annually are lost by self-employed arthritic persons. Many persons who have arthritis attribute the arthritis to an injury, but actually there has occurred an exaggeration or acceleration of a pre-existing arthritis. They, too, stated that oftentimes arthritis may exist without the individual being aware of the condition.

Hench,⁹ in a review of 500 industrial accidents, considered 80 per cent of the patients to show degenerative arthritis, and 50 per cent of these attributed their industrial accidents as the cause of their disability. As a general rule, throughout the country, Workmen's Compensation Com-

missions hold that an injury that results in arthritis is justly and fully compensable.

CASE REPORT

The following case is an example of symptomatic aggravation of a pre-existing arthritis of the cervical spine by trauma.

The patient is a 57-year-old white man, who, on September 25, 1957, while driving his truck, was struck from behind by another truck, sustaining a "sudden snapping" of the neck. This was followed by pain in his neck and also at the base of his skull. X-rays taken the following day revealed rather extensive osteoarthritic changes, with narrowing between C-6 and C-7, and C-7 and D-1, associated with bony bridging between the last three cervical vertebrae. He was treated by means of physical therapeutic measures, and was able to continue with his work as a carpenter, with considerable difficulty in the use of his neck. When seen on December 1, 1958, he complained of considerable pain, stiffness, and limitation of motion of the cervical spine. X-rays taken on December 1, 1958, revealed extensive osteoarthritic changes involving the cervical vertebrae, associated with a bridging of the lower cervical vertebrae.

This case illustrates the aggravation of a pre-existing osteoarthritis of the cervical spine by a sprain-mechanism. The mechanism was prob-

ably that of the rather popular term "whiplash" injury of the neck. Inasmuch as the patient stated that he had no trouble with his neck prior to his injury, it can be assumed that the injury did aggravate the pre-existing arthritis. The factor of impending liability might well contribute to his continued complaints (figs. 10 and 11).

Factors to be considered in the evaluation of disability: (1) *Mobility*, is there a limited range of motion as a result of injury? (2) *Stability*, is the ligamentous apparatus intact, or are there ruptured ligaments that produce instability? (3) *Endurance*, can the joint withstand the amount of activity which it exhibited previously? (4) *Agility*, does the patient have the same capacity to coordinate the joint, the same skill in use, as was previously experienced? (5) *Competing power*, is the function in the joint limited to the point of influencing the patient's capacity to compete with others in carrying out his job? (6) *Strength*, what is the status of the musculature, full recovery or limited? (7) *X-ray evidence*, of alteration of joint surfaces.

Another situation may arise when a known symptomatic arthritis sustains an injury that may well aggravate his condition. The question in this type of case is: "Should he be entitled to all subsequent disability resulting from the arthritis?" It seems unfair from the viewpoint of

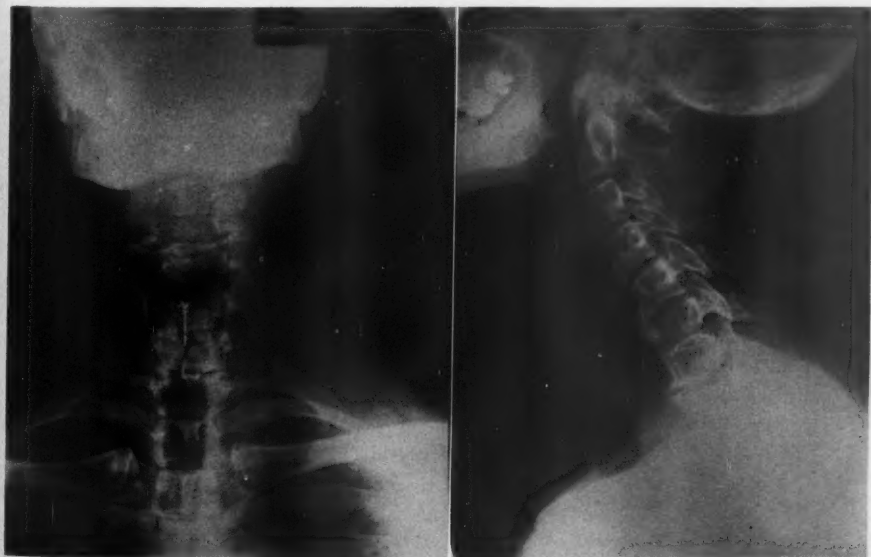


FIG. 10. X-rays of extensive osteoarthritic changes involving cervical spine. Day following injury

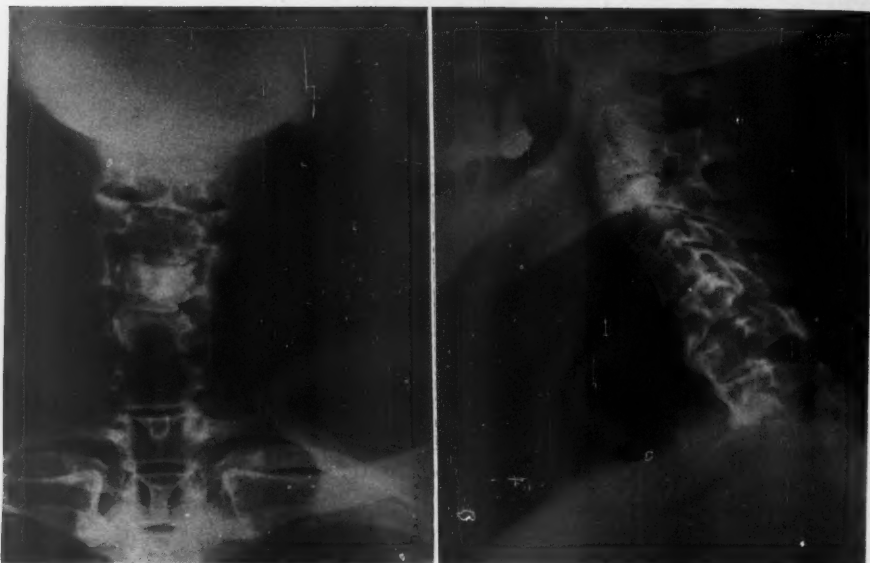


FIG. 11. X-rays, 14 months following injury, showing essentially the same degree of osteoarthritis

the insurance carrier, or the insured, to assume the responsibility for all future disability that might result from an aggravated arthritis, since it is fully appreciated that as a rule, the arthritic process is a slowly progressive one.

Another point to be considered is that arthritics go through a cycle when they have no symptoms. It has been estimated that most cases of arthritis in which trauma has been superimposed reach a "leveling off" period of from a half year to a year and a half.

SUMMARY

An attempt has been made to discuss the relation of trauma to arthritis. The difficulties encountered in evaluating this aspect of arthritis are included in the Discussion. There is no definite, objective, tangible "yardstick" to determine the extent or degree of aggravation of arthritis by trauma. That trauma can cause osteoarthritic or degenerative changes in a normal joint is admitted by various authors. The discussion and illustrations of the gross osteopathological changes in the more common types of arthritis have been included to assist in a better understanding of the problem.

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SOME CHEMICAL ASPECTS OF INFLAMMATION*

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Historically, the changes associated with inflammation and tissue repair have been of great interest to both the pathologist and the surgeon. Recently, the application of chemical rather than histochemical techniques to the study of the alterations in the connective tissue with respect to injury and repair has taken this important area of biology out of the special realm of the pathologist. It is of interest that this type of approach was first adopted by a surgical research unit.^{3, 11}

Recently, we have applied modified semimicro chemical techniques to the determination of the major components of the connective tissue in as little as 150 mg. of skin.^{5, 6, 8} The amount of collagen is precisely related to the concentration of the amino acid hydroxyproline;¹⁰ the quantity of ground substance is qualitatively determined by the amount of hexosamine;² and the total protein of a tissue may be calculated by measuring the nitrogen content.

In this paper, we will discuss the application of these chemical methods to different tissues of the body, and describe some of the changes in chemical analysis associated with the inflammatory response.

MATERIAL AND METHODS

The animals employed in these experiments were Sprague-Dawley rats grouped according to body weight. To provide controlled areas of necrosis, croton oil (Magnus, Mabce and Reynard Co., N. Y.) was injected intradermally, either after dilution with an equal volume of peanut oil or without dilution, into a previously shaved area of rat skin. The intensity and depth of the necrotic lesion so produced was generally proportional to the concentration of the croton oil, whereas the surface area involved was about the same for both the diluted and undiluted irritant. No aqueous soluble material of any

physiologic activity is extractable from this preparation of croton oil (Houck, unpublished), so all chemical changes are in response to the local injury. The irritant produced a necrotic area of about one cm.² within 3 days for the diluted croton oil and within 48 hr. after using the undiluted material. The injury produced a defect in the skin including the dermis, epidermis, fascia and the subcutaneous muscle. These latter tissues were much more involved when the irritant was undiluted. Two types of injury occurred with the two concentrations of the croton oil: (1) the diluted material produced a necrotic area which was rapidly isolated by inflammation forming an eschar within 4 days; and (2) the stronger irritant produced an injury which was too intense to be rapidly isolated, and the eschar took 7 days to form. The former eschar sloughed within 7 days and the wound healed by 14 days. The latter injury took 17 days to slough and was healed by the 24th day.⁸

The experimental design was as follows: A number of rats were shaved on one side, injected with 0.4 ml. of irritant, and at various days after injury the animals were sacrificed in groups of six by etherization. Both the injected area and an area of the opposite side of the animal were removed, along with 5 ml. of blood. This tissue was carefully dissected clean of adherent fat and muscle, and stored in a frozen state. After thawing, tissues were weighed, minced and autoclaved with 10 ml. per gm. of 4 N NHCl for 3 hr. The samples were then incubated at 100°C for 2 hr., at which time duplicate 0.1-ml. samples were removed for nitrogen and hydroxyproline determination. After 5 hr. of incubation, 1-ml. samples were removed for hexosamine analysis. These heating times were optimal for hydrolysis to free hexosamine and hydroxyproline, whereas quantitative recoveries of these compounds could be effected from the tissue mixture. The results of these analyses were expressed in μ moles per gm. of fresh, wet, tissue.

Analysis for hexosamine. The 1-ml. samples were neutralized with 4 N NaOH and diluted

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with 2 ml. of acetylacetone carbonate reagent and 1 ml. of 4 N NaCl. This mixture was treated according to Blix.¹ The results were translated *via* a standard curve into μ moles per gm. of fresh tissue.

Analysis for nitrogen. The appropriate 0.1-sample was diluted 300-fold with water and 0.1 ml. of this solution was mixed with 0.2 ml. of a digestion mixture of 50 per cent sulfuric acid containing 1 per cent SeO_2 . After digestion this mixture was diluted to 7 ml. with water, and 3 ml. of Koch-McMeekin's Nessler solution were added. The resulting optical density at 430 $m\mu$ was translated *via* a standard curve into μ moles per gm. of fresh tissue.

Analysis for hydroxyproline. The 0.1-ml. samples were diluted to 2.5 ml. with a 4 N HCl. Of this solution, 0.5 ml. was diluted to 5 ml. with water and 1-ml. samples were then analyzed for hydroxyproline by the method of Martin and Axelrod.⁹

EXPERIMENTAL AND RESULTS

Obviously, the percentage of fat and water in the skin will vary considerably with the location of the tissue sample and the dietary state and age of the animal. Therefore, the results of the analyses described above will be in considerable error if expressed in terms of μ moles per gm. of tissue. Consequently, Dunphy and Udupa³ and others extracted the tissue before analysis with lipid and water solvents and based their results upon the weight of the desiccated, defatted tissue. For small amounts of tissue, this method is not practical. We have found that by expressing our results in terms of the ratio of μ moles of either hexosamine or hydroxyproline to mmoles of nitrogen, there is no variation in analysis with the location of tissue sample. To demonstrate the

homogeneity of the chemistry of the skin when the data are expressed relative to the total protein, 12 rats weighing about 300 gm. were sacrificed and skin samples from the dorsal, ventral, and right foreleg and left hindleg areas were analyzed. The results, shown in table 1, indicate that there is no statistically significant variation in chemical analysis with skin locality, confirming a previous report.⁸

Table 2 illustrates the analytic values for a variety of human tissues. The analytic results for the skin of rachitic rats, obtained from the Department of Agriculture Laboratories, indicated that the animals should weigh about 200 gm., as previously reported.⁵ The mean weight of these animals, however, was 70 gm.

Figure 1 shows the alterations in both the injured tissue and in the skin opposite the site of injury. The decrease in the hydroxyproline content of the uninjured tissue was found with both the concentrated and the diluted irritant. There is no apparent histologic evidence for this reduction in collagen. Histologically, however, there is little collagen remaining in the necrotic areas despite the presence of some 40 per cent of the total hydroxyproline. There is considerable reticulin observable at the site of injury, however, and this material is similar to procollagen⁷ and has the same amino acid analysis as does collagen itself.⁴ There is no systemic response to local injury with respect to the concentration of ground substance, however.

Table 3 indicates a profound difference in the appearance of hydroxyproline-containing polypeptides in the serum with dilution of the irritant. The hydroxyproline-containing serum is found only with injury produced by the concentrated irritant. This serum material was precipitable in 50 per cent ethanol and must be a polypeptide.⁸

TABLE 1
Mean chemical ratios of various skin areas

Ratio*	Skin Locations			
	Right foreleg	Left hindleg	Ventral	Dorsal
Hexosamine:nitrogen	4.1 \pm .9	3.7 \pm .2	3.8 \pm .7	3.8 \pm .6
Hydroxyproline:nitrogen	116 \pm 52	110 \pm 18	117 \pm 19	120 \pm 28
Hexosamine:hydroxyproline	.024 \pm .005	.024 \pm .004	.026 \pm .005	.023 \pm .003

* Ratios are expressed in terms of μ moles of either hexosamine or hydroxyproline to mmoles of nitrogen.

TABLE 2
Mean chemical analysis of various tissues

Tissue	Number	OH _p :N*	H:N†
Human skin (adult).....	21	110.6	2.6
Human skin (Mongoloid children).....	8	50	2.3
Human fascia.....	8	135.8	3.9
Human aorta.....	12	73.1	13.1
Rat skin (normal, 200 gm.).....	24	120	3.9
Rat skin (rachitic, 70 gm.).....	10	119	4.1

* Hydroxyproline (μ moles):nitrogen (mmoles).

† Hexosamine (μ moles):nitrogen (mmoles).

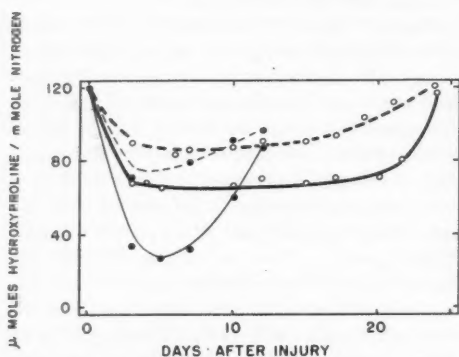


FIG. 1. The changes in the ratio of hydroxyproline to nitrogen of the uninjured skin (broken line) and the necrotic area (solid line) at various days after injury by concentrated (○) and diluted (●) croton oil. All values are the mean of 6 animals analyzed in triplicate.

TABLE 3
Hydroxyproline to nitrogen ratios of rat serum following injury

Days After Injury	Ratios	
	Concentrated irritant	Diluted irritant
0	1.2	1.3
3	7.0*	1.21
4	7.1*	—
5	10.8*	1.44
6	12.2*	—
7	9.1*	1.71
12	6.0*	1.33
17	1.4	—

* Statistically significant elevations ($p < 0.01$).

DISCUSSION AND SUMMARY

As has been discussed in detail elsewhere,⁸ the decrease in the hydroxyproline concentration of uninjured skin must be in response to the local inflammation, because there is no variation in the chemistry of rat skin with respect to tissue location. Despite the systemic response, which is approximately equivalent for both diluted and undiluted concentrations of irritant, only the more intense injury was associated with a parallel increase in serum hydroxyproline. In addition, this injury did not result in as impressive a quantitative reduction of hydroxyproline at the site of injury as did the diluted croton oil.

One possible explanation for the similar systemic response with both irritants would be that this reaction to local injury is independent of the extent of the wound, but is automatically potentiated by necrosis of a sufficient "threshold" size. The lack of hydroxyproline release into the serum would then mean that this phenomena might not be associated with the systemic decrease in total hydroxyproline, but with the local disappearance of this amino acid from the area of injury. Owing to the rapid isolation of this area from the surrounding tissue, and the consequently swift formation of an eschar, the products of the less intense injury would not reach the circulation so easily as the more profound injury. Similarly, the more extreme reduction in local hydroxyproline with the injection of the diluted irritant could well be due to a less extensive release of neutralizing and healing components from the blood into the necrotic area. The eschar of these wounds sloughed more readily, thus removing the irritant, since the intensity and depth of injury were such that a rapid isolation and disposal of the necrotic tissue was possible. The more concentrated irritant produced more injury, and the amount of tissue directly and indirectly involved was so relatively more extensive that the host could not isolate and slough the necrotic area as readily. In the former case then, the host must simply dispose of the necrotic area, whereas in the latter situation there must be a neutralization of the irritant and a partial restoration of local tissue reserves before sloughing. Therefore, when the stronger irritant was used, the exchange between circulation and the necrotic area was greater. The body defense materials would then limit the extent of local injury, whereas the drainage of necrotic materials might then be sufficiently in ex-

cess of the ability of reticuloendothelial system and lymphatics to handle, and some of this material would spill over into the serum. The less intense injury would not require the blood elements for partial tissue restoration before sloughing, and hence the more extensive reduction in local hydroxyproline. In this case, however, the lymphatic system would be able to handle the drainage of local necrotic materials without "spillage" into the serum.

The systemic loss of hydroxyproline would not be necessarily produce histologic evidence of its occurrence, since the more soluble collagen or procollagen is found on the surface of the fibers.⁷ The loss of this material would not necessarily alter the tinctorial or structural appearance of the fibers. The drainage of this material could also occur *via* the existing lymphatic systems.

Essential to the acceptance of this highly presumptive theoretic discussion would be the demonstration of changes in the hydroxyproline content of the reticuloendothelial system of the injured animals. The major assumption made in this discussion is that the reticuloendothelial cells sequester the hydroxyproline-containing polypeptides released during inflammation. These cells might then be expected to differ in both analysis and properties from the normal reticuloendothelial cell. Experiments along these lines are currently underway. Studies of the results of attempts to modify the course of inflammation by the use of local and other blocking agents such as Pontocaine and atropine are also being undertaken.

The necessity for the surgeon to have some understanding of the basic mechanisms and the chemistry of the healing process is obvious. The

authors believe that similar information with respect to the inflammatory response is also essential. It is hoped, therefore, that the foregoing data and the theoretic speculation will at least point out the need of continued investigations in this field of interest.

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REGENERATION OF URINARY BLADDER AFTER SUBTOTAL RESECTION FOR CARCINOMA*

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We have demonstrated that after subtotal cystectomy in the dog, the entire bladder wall regenerated. We first reported clinical use of this remarkable regenerative ability of the urinary bladder in 1953.¹ In the human, as well as the dog, the new bladder is composed of all layers seen in the normal bladder. From a clinical standpoint, regeneration always occurs unless the urine is diverted from the area. The regeneration into the form of a hollow viscus is apparently due to an unknown chemical inductor in the connective tissue matrix immediately beneath the epithelium of the urethra at the vesical neck, or the terminal ends of the adjacent ureters or both. This paper reports nine years' experience with the procedure in 70 patients.

PROCEDURE

In order to study the procedure of subtotal cystectomy and bladder regeneration, cancers at various sites in the bladder and of varying stage and grade were included in the series on an unselected basis. All patients with papillomas were excluded because these are not cancers. Treatment was classified as palliative only when the cancer had spread beyond the bladder to the pelvis or to multiple lymph nodes, or chest or bones.

A diagnosis of carcinoma was established in each patient by a transurethral resection of the entire lesion with the patient under general anesthesia. This general rule of complete transurethral resection of the lesion was adhered to throughout the study with the exception of huge bladder carcinomas. In this latter situation, biopsies of multiple areas were performed with the resectoscope. Following resection of the carcinoma, the entire base of the lesion including a 1-cm. margin peripheral to the edge of the lesion was electrocoagulated. Subtotal cystectomy was performed

4 to 7 days later. Based on location, size and depth of infiltration of the carcinoma, varying percentages of the bladder were removed. The precise amount of excision had to be determined at time of operation because endoscopic appearance and bimanual examination were of little assistance. Lesions of low grade and low stage usually resulted in excision of only about 30 to 50 per cent of the bladder. Lesions of moderate grade and moderate stage which were larger in circumference, were excised by subtotal technique in which all but a piece of the bladder was removed. Regardless of amount of vesical excision, whenever possible a small piece of the bladder was salvaged since it accelerated regeneration and resulted in a larger definitive bladder. In all patients the peritoneum attached to the bladder, the perivesical fat and the bladder segment were removed *en bloc*.

As the objective of the operation was to excise cancer, no attempt was made to salvage one or both ureteral orifices if so doing would appear to compromise adequate excision of the lesion. Consequently, one or both of the orifices were often sacrificed. The ureter or ureters were reanastomosed to the remaining bladder segment just before complete closure of the segment. A standard fishmouth ureterocystoneostomy was performed.

In most patients it was possible to close the remaining bladder segment, regardless of its shape, over an inflated 5-cc. bag of a Foley catheter. In some 12 patients, it was impossible to close the residual bladder segment because of its small size. In these patients the ends of the ureter or ureters were spatulated and anastomosed to the edge of the residual piece of bladder with a single suture. In a few patients with lesions at the vesical neck even this small bladder segment had to be excised, thus performing total cystectomy. The ureters of these latter patients were managed in one of two ways: A large isolated segment of rectosigmoid was anastomosed to the urethra, the proximal end of the segment was closed and the ureters were sutured into this

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piece of bowel. Continuity of colon was established with the standard end-to-end closure. In several male patients, however, true total regeneration of the bladder developed as the ends of the ureters were spatulated, and by a single suture each was attached to the anterior rectal wall as close as possible to the urethra. We prefer the isolated rectosigmoid anastomosis to this latter method, however, because of the shorter complete convalescence of the patient.

In all patients an empty Penrose drain was inserted through the abdominal wound to the bladder or the bladder area. As the pelvic peritoneum had been excised with the lesion, the pelvic floor could not be reperitonealized in any of the patients. The Penrose drain was removed approximately 4 to 7 days after suprapubic urinary drainage had stopped and 1 day after removal of the urethral catheter. If suprapubic drainage persisted for longer than 14 days, the drain was removed. The catheter was left in place for 4 to 7 days after suprapubic drainage ceased.

RESULTS

Essentially this method of management of bladder cancers consists of two surgical procedures: a preliminary complete transurethral resection of the lesion followed by a subtotal cystectomy. It has been of interest to study these subtotal cystectomy specimens. Such specimens of some superficially infiltrating lesions, as determined by the earlier transurethral resection, have later demonstrated that tumor cells were present in the adventitial lymphatics or in the lymphatics of the bladder wall some distance from the site of the original lesion. It was particularly disquieting to observe cancer cells in adventitial lymphatics when meticulous search of the transurethral resected cancer site failed to reveal any residual cancer. Although only a few such cases were observed in this study, they represent definite, conclusive failure of cure by transurethral resection of superficial infiltrating cancer. These patients tend to support our earlier observations relative to the circumferential spread of cancer within the lymphatics of the bladder wall.^{2,3} These findings also prompted institution of our existing program in which peritoneum and perivesical fat as well as the bladder segment with its tumor are removed in a block, since this fat

or adventitia surrounding the bladder may contain cancer cells.

No intestinal complications resulted from inability to reperitonealize the pelvis. Peritonitis did not complicate the postoperative course. Ileus has been a troublesome factor in several patients but has never been greater than that observed in certain individuals following routine renal surgery. Early in the study 2 ward patients probably developed unsuspected electrolyte imbalance which became fatal. Electrolyte imbalance is assumed since no demonstrable cause of death was detected at autopsy. No subsequent ward or private patients have died from electrolyte imbalance. No electrolyte imbalance has been observed that has required treatment. One private patient with a deeply infiltrative squamous cell carcinoma died of a pulmonary embolus approximately 8 weeks after subtotal cystectomy.

Most patients were sent home 10 to 18 days after surgery while still draining urine suprapubically. As might be expected, the less bladder excised, the sooner the patients were discharged from the hospital. The urethral catheter usually drained very little for the first week or two postoperatively. Most patients stopped draining urine from the suprapubic wound within 3 to 5 weeks after surgery. Two patients having total cystectomy without ureteral transplantation drained urine slightly, in excess of 4 months. All patients regenerated a new bladder which closed spontaneously.

One of five patients (20 per cent) developed some degree of ureterorenal reflux. This has on occasion been accompanied by minimal to moderate degrees of ureteral dilation and hydronephrosis. The ureterectasis and pyelectasis usually decreased, once definitive bladder size was attained. Although ureterorenal reflux has been observed as part of this study, with 9 years' experience with the procedure it has not presented a clinical problem except in one instance. That patient had severe, recurrent pyelonephritis which required vigorous antibiotic and chemotherapeutic drug therapy. It should also be reported that ureterorenal reflux can develop in a ureter which has not been disconnected and reanastomosed to the bladder. The significance of this observation is not clear but is under study at present.

Nocturia and diurnal urinary frequency were marked, from 1 to 2 months postoperatively. At

the end of 4 to 6 months, none of the patients in the series had nocturia of more than two to three times each night. During the day, none voided more frequently than once every 2 to 3 hours. Cystographic appearance of the bladder demonstrates a viscus which is quite irregular. Cystograms taken at 4, 6 and 12 months show that there is an increase in bladder size from the 4th to the 6th month. Bladder capacity probably does not increase appreciably after 12 months. The mean bladder capacity for the patients studied ranged between 175 to 410 cc. of urine. The patient with 175 cc. of bladder urine capacity had total cystectomy with complete bladder regeneration. Only 1 patient in every 10 to 15 will have any residual urine. Residual urine has never been measured at more than 20 cc.

In all patients, regeneration of the bladder occurred. In only 1 patient was the bladder capacity exceedingly small; this was in a person 79 years of age. In a personal communication Lewis⁵ has also noted that patients of the very old age group regenerate with a small bladder capacity after a subtotal cystectomy.

The total number of patients with tumors of a particular stage and grade who have been followed for a full 5-year postoperative period is too small to permit standard statistic comparison with other methods of management at this time. It can be stated, however, even when postoperative mortality is considered, that the results are equal to or better than those achieved with either transurethral resection or total cystectomy.

It has been possible to obtain full thickness biopsy of the regenerated bladder *via* the suprapubic route. Photomicrographs of the regenerated bladder demonstrate fibrous tissue interlaced with muscle fibers. These muscle fibers are not always continuous through the bladder wall, but originate as separate isolated muscle fibers in the fibrous bladder sheath. The presence of muscle in the regenerated bladder undoubtedly accounts for the notable lack of residual urine in all but a few of the patients studied. The fact that the muscle fibers initiate at individual sites within the fibrous tissue tends to support the view that muscle fibers are not an extension of ureteral or urethral musculature. Apparently the proximity of the urethra and ureters serves as an inductor phenomenon for development of muscle fibers from the totipotent mesenchymal-fibroblastic cell.

Patients who had extensive lesions of the bladder were also subject to subtotal cystectomy as a palliative procedure. It was found that eliminating the tumor mass and reanastomosing the ureter to the residual bladder made these patients considerably more comfortable. In addition, the patients had the distinct advantage of being able to void *via* normal channels rather than by using urinary or colostomy collection bags attached to the abdominal wall. In several patients the huge cancer had involved the bony walls of the pelvis and subtotal cystectomy could not be used. It is our opinion that very little could have been accomplished by any other type of surgical procedure with this type of advanced bladder cancer.

It was not expected that any of the patients with advanced bladder cancer treated by total cystectomy would be cured of their disease. It should be added, however, that several of them are alive 4, 5 and 8 years after subtotal cystectomy and are to date clinically free of cancer.

DISCUSSION AND SUMMARY

The percentage of patients having bladder cancer which is potentially curable by transurethral or suprapubic segmental resection should be increased by use of subtotal cystectomy. The results of transurethral resection cannot be improved upon as a curative method since not even the full thickness of bladder beneath the tumor can be excised for fear of perforation of the bladder. Regardless of stage or grade, the older, classical segmental resection cures more patients than does the transurethral resection. Present statistics indicate that standard segmental resection effects a 5-year survival rate equal to that of simple cystectomy (tables 1 and 2). It is certainly possible that those patients cured by total cystectomy could reasonably be expected to be cured by subtotal cystectomy. Of great importance to the patient is the fact that with subtotal cystectomy the ureters are not transplanted elsewhere than to the bladder. As a consequence, these patients void *via* the urethra with full urinary control.

Subtotal cystectomy should be considered as a large segmental resection in which ureteral orifices are not spared at the expense of leaving cancer cells within the bladder. Subtotal cystectomy is a simple procedure which can be performed readily at any hospital by any urologist.

Many urologists do not like suprapubic seg-

TABLE 1

Five-year survival rates in deep infiltrating carcinoma

	%
Electroexcision	
Nichols.....	15
Milner (B ₁).....	23
Flocks (B ₂).....	3
Milner (C).....	7
Average.....	12
Standard segmental resection	
Marshall.....	22.0
Jewett.....	8.3
Average.....	15.1
Simple cystectomy	
Brice.....	10.9
Jewett.....	9.0
Average.....	9.9

TABLE 2

Five-year survival rates in superficial infiltrating carcinoma

	%
Electroexcision	
Nichols (A).....	81.4
Milner (A).....	70.0
Milner (B ₁).....	57.0
Flocks (B ₁).....	56.0
Average.....	67
Standard segmental resection	
Marshall.....	62.5
Jewett.....	70.0
Average.....	66.3
Simple cystectomy	
Brice.....	36.8
Jewett.....	50.0
Average.....	43.3

mental resection because it is felt that manipulation of the tumor cells can disseminate these cells outside the bladder. This objection was eliminated in this series by preliminary transurethral resection of the entire lesion before subtotal cystectomy.

Deeply infiltrating lesions at the vesical neck are probably not suitable candidates for subtotal cystectomy. These patients as well as those with proved multifocal cancer undoubtedly require total cystectomy. As described above, this does not imply that ureters must be diverted elsewhere.

Subtotal cystectomy is sometimes associated with prolonged suprapubic urinary drainage, however, this is no objection to the procedure; with cystectomy and transplantation of the ureters to an ileal pouch, there is *permanent* urinary drainage from an opening on the abdominal wall.

Urologists who perform lymphadenectomy at the time of cystectomy will find some difficulty if subtotal cystectomy is used. In essence, the remaining bladder segment is in the way of the operator. Lymphadenectomy can be performed with subtotal cystectomy as completely and efficiently on the side containing the tumor as when total cystectomy is employed.

The 20 per cent incidence of ureterorenal reflux after subtotal cystectomy may appear as a major complication. It has not been so. We are well aware of the disadvantage of ureterorenal reflux, having been among the first to investigate and report on reflux after ureterointestinal anastomosis.⁴ To date, the only adverse clinical effect of reflux we have seen, occurred in a patient with a severe unilateral pyelonephritis; this effect is considerably less than has been seen with any type of ureteral transplantation. Furthermore, the incidence of radiographic renal and ureteral abnormalities is greater after any type of ureterointestinal anastomosis than the incidence of reflux in patients after subtotal cystectomy. By preservation of the normal voiding mechanism, subtotal cystectomy has advantages that do not require further discussion, and that outweigh any of the complications that have been encountered during 9 years' experience with the procedure.

The use of subtotal cystectomy in patients with far advanced bladder cancer appears to be worthwhile as a palliative procedure since it removes the large, irritating and often bleeding mass. As the procedure permits reimplantation of an involved ureter to a normal segment of the bladder, these patients void with normal urinary control. In most patients with far advanced bladder cancer, the procedure, when it can be used at all, is preferred by us to any other that we have previously employed.

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CARCINOMA ARISING IN THE GASTRIC STUMP FOLLOWING
GASTRIC RESECTION FOR BENIGN ULCERATION

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Although recurrent carcinoma of the gastric stump following resection of the stomach for primary carcinoma is by no means uncommon, the development of carcinoma in the gastric stump following resection for benign ulceration has heretofore been considered a rarity. This belief was based largely on the fact that the part of the stomach which is most commonly the site of carcinoma, namely the middle and distal third, is removed in the conventional resection for benign ulceration. Furthermore, the thought has become well established that a history or the existence of a duodenal ulcer, which is the commonest indication for gastric resection, provides real protection against the development of neoplastic disease in the stomach.

However, sporadic case reports of the occurrence of this complication led to a collection by Freedman and Berne,² in 1954, of 58 such cases, including 3 of their own. These authors estimate the incidence of this complication as being approximately 1 per cent after gastric resection for benign ulcer. In their collected cases it was evident that carcinoma develops in the region of the gastroenteric stoma in the majority of cases, and may be easily confused with benign anastomotic ulceration. Inasmuch as it had been suggested that this incidence of carcinoma was not greater than the expected statistic incidence in this age group, and therefore not directly related to the previous gastric resection, Helsing and Hillestad,³ in 1956, studied a group of 222 cases of gastric resection over a long period of time. Of these, 11 developed carcinoma in the gastric remnant. This represented more than double the predicted incidence of carcinoma naturally occurring in this group. In a more detailed analysis of their material, it was found that after gastric resection for gastric ulcer the observed frequency

was three times greater than the expected incidence, whereas in the group operated for duodenal ulcer the expected and observed frequencies were identical. Subsequently, Krause⁴ studied 361 patients in whom a high resection with Billroth II anastomosis had been carried out. Of the 210 patients in this series who had died, 25 were found to have carcinoma of the gastric stump, the statistic expectancy in this group being 11.3. The interval between gastric resection and the development of carcinoma ranged from 8 to 28 years, the mean being 20 years. In this series there appeared to be no greater incidence of carcinoma following resection for gastric ulcer than for duodenal ulcer. However, in the series of 15 cases studied by Côté and associates¹ it appeared that the likelihood of this complication is considerably greater after surgery for gastric ulcer than after the operative treatment for duodenal ulcer. In their series carcinoma developed after gastric resection in 5 cases, and in 10 cases after gastrojejunostomy with excision of a gastric ulcer. These authors noted a remarkably low degree of cellular anaplasia in this group of carcinomas, 6 of the 15 being graded 2.

It appears that in the light of the available evidence the statistic chance of a carcinoma developing in the gastric stump after gastric resection for benign gastric ulcer is considerably increased, although this same danger does not appear to follow resection for duodenal ulcer. Numerous factors have been suggested to explain this complication. Achlorhydria with associated atrophic gastritis, hypertrophic gastritis, and polypoid changes in the gastric mucosa have all been observed.⁶ Exposure of the gastric mucosa in the region of the stoma to the alkaline duodenal juices has been suggested as the mechanism. Malignant degeneration of a pre-existing benign stomal ulcer has been offered as an explanation. Careful pathologic study of the resected gastric remnant has in no reported instance revealed any change suggesting a precancerous lesion. Although the gastric pouch, following resection for

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duodenal ulcer, is not completely immune to the development of carcinoma, it would appear that this is not greater than the expected incidence; and probably is less. Ransom⁵ was able to collect only 5 such cases in a review of the literature.

During the past several years 3 cases in which carcinoma developed in the gastric pouch following resection for benign gastric ulcer have been encountered by us. Since each of these presents distinctive problems, the 3 cases will be reported individually.

CASE REPORTS

Case 1. A. A. I., a white man aged 48, was admitted to Georgetown University Hospital on October 19, 1958, with a chief complaint of epigastric distress of 1 year's duration. A gastric resection for a benign gastric ulcer had been carried out elsewhere, 30 months previously. This procedure consisted of resection of 70 per cent of the stomach with a Billroth II anastomosis. Eighteen months later he developed epigastric discomfort and recurrent fullness after meals. During the past 6 months severe episodic attacks of vomiting occurred. Upper gastrointestinal studies revealed the presence of a stomal ulcer with marked dilation of the afferent loop (fig. 1). On gastroscopic examination severe gastritis with thickened, reddened folds was observed in the region of the gastrojejunostomy; however, no ulceration was seen. A clinical diagnosis of stomal ulceration with afferent loop obstruction seemed evident.



FIG. 1. Marked dilation of afferent loop (Case 1)

After adequate preoperative preparation, surgical intervention was carried out on October 20, 1958, under general anesthesia. A large indurated mass, measuring 8 cm. in diameter, involved the distal stomach, the midtransverse colon, and the area of the retrocolic gastrojejunostomy. With considerable technical difficulty the anastomosis was dissected out of the transverse mesocolon, and the involved jejunum and distal stomach were resected. After completing an end-to-end jejunojunostomy, a subdiaphragmatic vagotomy was carried out and the residual stomach was anastomosed to the anteromedial aspect of the descending duodenum. The report of pathologic examination revealed the surprising finding of an infiltrating small cell carcinoma of the stomach in association with severe chronic gastritis. The gross appearance of the specimen had in no way suggested this neoplastic disease.

After a relatively uncomplicated postoperative course, he was discharged from the hospital on the 14th postoperative day and has remained relatively asymptomatic since then.

A review of the pathologic material from the previous resection showed only a benign ulcer.

Case 2. T. H., a white man aged 57, was admitted to the Georgetown Surgical Service, District of Columbia General Hospital on December 10, 1958, because of persistent vomiting, weakness and syncope. Twenty-eight years previously the patient was subjected to a high gastric resection with a Billroth II anastomosis because of a perforated gastric ulcer. In spite of being a chronic alcoholic, he had remained asymptomatic until 19 months previously at which time he developed intermittent upper abdominal distress, unrelieved by food. An upper gastrointestinal study 3 months previously revealed "two small gastric ulcers." During the past 3 months symptoms persisted in a less severe form, and there was associated anorexia and a weight loss of 13 pounds. During the past week persistent vomiting had developed.

Physical examination was not remarkable except for evidence of some weight loss. Before admission, an upper gastrointestinal x-ray study revealed a markedly dilated stomach with notable dilation of the afferent loop (fig. 2). On December 27, 1958, surgical intervention was carried out. An indurated mass was found at the site of the antecolic anastomosis between the stomach, of which 40 per cent had been resected, and a long loop of jejunum. A suspicion of neoplastic change in the gastric remnant was mentioned at the time of the operative procedure. The stomach was resected to the extent of about 70 per cent and, after reconstruction of the jejunum, a new antecolic gastrojejunostomy was carried out. Pathologic examination revealed a poorly differentiated



FIG. 2. Dilation of both afferent loop and residual stomach (Case 2).



FIG. 3. Gastric resection with normally functioning gastrojejunal anastomosis (Case 3).

adenocarcinoma of the stomach which had invaded the gastric wall, the lymphatics and had spread to the regional lymph nodes. After an uncomplicated postoperative course, the patient was discharged on the 18th postoperative day.

The pathologic material obtained at the time

of the original gastric resection was not available for study.

Case 3. W. C., a white man aged 44, was admitted to Georgetown University Hospital on November 16, 1946, because of severe upper abdominal pain, nausea and vomiting. Because free air was found under the left diaphragm, a diagnosis of perforated peptic ulcer was made and the patient was immediately operated upon. A perforated ulcer was found on the posterior wall of the stomach and a resection of 65 per cent of the stomach with an anterior gastrojejunostomy was performed.

In 1952, because of the identification of a microcytic anemia, he received vitamin B₁₂ without significant response. Subsequently several transfusions were administered.

In March of 1955 an episode of tarry stools associated with aggravation of the pre-existing anemia was observed. Upper gastrointestinal x-ray studies failed to demonstrate any lesion at that time. Gastroscopy revealed hyperemic edematous gastric mucosa.

On December 14, 1956, he was again hospitalized because of hematemesis requiring several transfusions. Again an upper gastrointestinal x-ray study was uninformative (fig. 3).

On June 20, 1956, he was admitted *via* the Emergency Room because of massive hematemesis associated with profound shock. The following day, because of continued bleeding, he was surgically explored. A large fungating, fixed mass was palpated in the gastric stump, densely adherent to the spleen and tail of the pancreas. This was considered to be neoplastic and a splenectomy, distal pancreatectomy, and total gastrectomy were carried out. A Roux-en-Y esophagojejunostomy was created. Pathologic examination revealed the presence of adenocarcinoma of the stomach with metastasis to the jejunum and pancreas.

His postoperative course was characterized by increasing evidence of peritonitis, and he expired on the 4th postoperative day. Postmortem examination revealed acute generalized fibrinopurulent peritonitis secondary to necrosis and leakage of the esophagojejunostomy. Residual carcinoma was identified in the head and body of the pancreas and in the periaortic lymph glands.

DISCUSSION

Although the occurrence of 3 cases of carcinoma of the stomach following resection for benign gastric ulcer in our institution during a relatively brief period of time has no statistic significance, it suggested to the authors that this is more than a coincidental occurrence. A review of published data related to this question lends support to this

impression. It is, furthermore, somewhat significant that in no instance in our material has this complication been observed following resection for duodenal ulcer. It is interesting that in these cases and in practically all of the reported cases this complication has been associated with a gastrojejunal type of anastomosis, and in the majority of cases the carcinoma has been stomal in location. It is noteworthy that a report of this complication following a Billroth I type of anastomosis after gastric resection for benign gastric ulcer has not been encountered in any instance. Whether this is the result of the more limited use of the Billroth I procedure or whether it indicates a lowered incidence of carcinoma following a gastroduodenostomy as compared to gastrojejunostomy is questionable. In any event the facts suggest that whatever factors are responsible, the stomach adjacent to the gastrojejunal anastomosis is the site of predilection. It is also deserving of comment that the incidence of carcinoma following gastrojejunostomy for gastric ulcer without resection would appear to be greater than that of expected statistic occurrence.

In the 3 cases reported herein the histopathology of the tumor was of the usual degree of anaplasia, and a lower degree as observed by Côté and associates¹ was not encountered. In two instances the carcinoma was not grossly evident, and in both instances recognition depended on histopathologic identification. In the third case the carcinoma was obvious. In all three instances the carcinoma was immediately adjacent to or in the vicinity of the gastrojejunal stoma, and in two, the stomal obstruction had resulted in a conspicuous dilation of the afferent loop as demonstrated by roentgenologic study. The interval between resection and the development of carcinoma in our cases was 30 months, 10 years and 28 years. The objection might be raised that in the first case in which a relatively short interval existed the carcinoma may well have represented a recurrence of a lesion present at the time of the original resection. However, careful and painstaking review of both the ulcer and the distal edge of the resected specimen revealed no evidence of cancer or precancerous change.

A preoperative diagnosis of carcinoma was not made in any of these cases and, as is usually the case, the clinical diagnosis was "marginal ulcer." In 2 of the cases, gastroscopy was carried

out and the only change noted was the presence of a hypertrophic hemorrhagic gastritis, in both instances. It is interesting that in 2 of the cases a conspicuous distention of the afferent loops was demonstrated by x-ray means, and in both cases some of the clinical symptomatology suggested an afferent loop syndrome. A gastric analysis was not obtained in any of the 3 cases.

An analysis of these 3 cases together with consideration of the published data relating to this complication of gastric resection for benign ulceration suggests three distinct points: (1) Clinical and roentgenologic evidence of afferent loop obstruction following gastric resection should suggest the possibility of the development of stomal carcinoma as the cause. (2) In view of the slight incidence of anastomotic ulcer following gastric resection for benign gastric ulcer, the development of any clinical or roentgenologic evidence of such stomal ulceration should strongly suggest the possibility of carcinoma. (3) It would appear from a review of the available evidence that this complication is much less prone to develop following gastroduodenostomy than after gastrojejunostomy.

SUMMARY

Three cases of carcinoma of the gastric stump following resection for benign gastric ulcer are reported in detail. In addition the incidence, mechanism and other features of this complication are reviewed.

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SURGICAL IMPLICATIONS OF MEDIASTINAL GRANULOMAS

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For years granulomatous lesions of the mediastinum provoked only the barest mention in the medical literature, giving rise to the impression that they were of rare occurrence and no great consequence. Since 1950, however, there has been a mounting interest in these lesions as attested by the publication of a number of papers emphasizing both their clinical and surgical significance.^{1, 3, 5, 6, 11-13} Recently we have published such a report suggesting among other things that granulomatous tumors of the mediastinum are far from uncommon.⁹ The present study is an extension of this earlier report and is based on personal experience with 25 mediastinal granulomas from which histologic material is available, a series larger than any previously reported.

INCIDENCE

It is nearly impossible to assess accurately the frequency of occurrence of mediastinal granulomas, although they are clearly more common than past evidence would indicate. For example, in a general review of primary mediastinal tumors other than lymphomas it was found that granulomas constituted only 1.5 per cent of the total.⁸ On the surface this figure should represent a reliable estimate of the incidence of granulomas relative to other tumors of the mediastinum, for it is based on a large and unselected group of 855 mediastinal tumors, only 13 of which were recognized as granulomas.⁸ However, there is room for argument here, considering that the 25 cases included in this report have been culled from a total experience limited to approximately 200 primary mediastinal tumors (12 per cent). Obviously the percentage of granulomas can be influenced by one's interest in and awareness of the lesion. We assume that by conservative estimate granulomas probably represent between 5 and 10 per cent of all primary mediastinal tumors,

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and that as interest grows, there will be fewer cases mislabeled and more recognized as granulomas.

Location. Inasmuch as any mediastinal lymph node can be the site of granulomatous involvement, there is a wide variation in the location of these granulomas. The classic site is the right paratracheal region just above the stem bronchus in the vicinity of the azygos vein and involving the so-called azygos lymph nodes. Sixteen of the 25 granulomas (64 per cent) in this series were so situated, lying alongside the trachea, superior vena cava and right vagus and phrenic nerves but anterior to the esophagus.

One patient presented with a left superior mediastinal component in addition to the right paratracheal lesion. In only two instances (8 per cent) did the tumor project solely from the left mediastinum. Five granulomas lay in the right posterior mediastinum adjacent to and usually compressing the esophagus. Most of these seemed to arise from the right subcarinal nodes. Of the two remaining granulomas, one involved the right hilus and the other was situated against the sternum just below the superior thoracic strait on the right side. This was the sole example in this series of an anterior mediastinal location.

In a general way the anatomic distribution of these cases is in keeping with that reflected in the literature, viz., the vast majority, certainly over 75 per cent, involve primarily the right mediastinum and of these most lie in a paratracheal, azygos node location.^{3, 5, 13}

Age, sex and race. Most of these patients were young adults, the youngest being 19. Only 6 of the 25 were over 35 years of age. The oldest was 54. As expected the sex distribution was even (12 women; 13 men). The white race predominated (4 Negroes).

PREOPERATIVE FINDINGS

Symptoms. In most instances the lesion is asymptomatic; 17 patients in this series had no symptoms referable to the mediastinal tumor

whereas 2 others had mild complaints (one a chronic cough, the other a vague precordial pain) that were probably unrelated to the tumor. One patient had a bothersome cough for 2 months before discovery of a right paratracheal tumor which was found at operation to be densely adherent to the trachea. Another patient presented with hemoptysis. Dysphagia led to the discovery of one paraesophageal granuloma while another was picked up in the course of a gastrointestinal series for evaluation of a "burning sensation" in the precordium. In fact, this aspect of the problem, namely, esophageal obstruction secondary to mediastinal granuloma, usually subcarinal in location, has been the subject of two recent publications.^{3, 7} Two patients manifested swelling of the face and neck secondary to superior vena caval compression. Dyspnea, chest pain and fever have also been attributed to these lesions.

Actually, considering the intimate association of these granulomas with the trachea, esophagus and superior vena cava, it is surprising that more of the patients do not have complaints.

Skin tests. Skin tests were not performed in all patients. Tuberculin skin tests were done in 15 and interpreted as positive in 5. Histoplasmin skin tests were obtained in 12 patients and were positive in 9. From skin tests alone one cannot make definitive etiologic diagnoses, but the results obtained in this group of cases correlated perfectly with subsequent pathologic and bacteriologic findings.

Radiographic findings. In most instances routine chest roentgenograms disclosed a mediastinal mass. The only exceptions were the two paraesophageal lesions, neither of which was visible on plain films. Each was well demonstrated by barium swallow, being delineated as a smooth extraluminal mass compressing and partially obstructing the esophagus (fig. 1). Usually the granuloma presented a circumscribed round, oval, or slightly lobulated margin projecting from the mediastinum. Typically the lesion extended from the right tracheal border much as the aortic knob extends from the left. Less commonly it appeared as a bulging, smoothly demarcated hilar (fig. 2) or subcarinal mass. The lateral view usually indicated a midcoronal position, but in one instance the lesion could be visualized immediately behind the sternum just inferior to the manubrial notch (fig. 3). On several occasions a



FIG. 1. Nonspecific granuloma obstructing esophagus in a 44-year-old white woman whose presenting complaint was dysphagia. Routine chest films were negative. Skin tests were not done. Barium swallow showed a tumor compressing the mid-esophagus. The mucosa appeared normal and the preoperative diagnosis was intramural tumor of the esophagus, probably leiomyoma. At operation it was found to be a 4-cm. granulomatous lymph node. Careful study of the excised specimen failed to reveal any organisms.

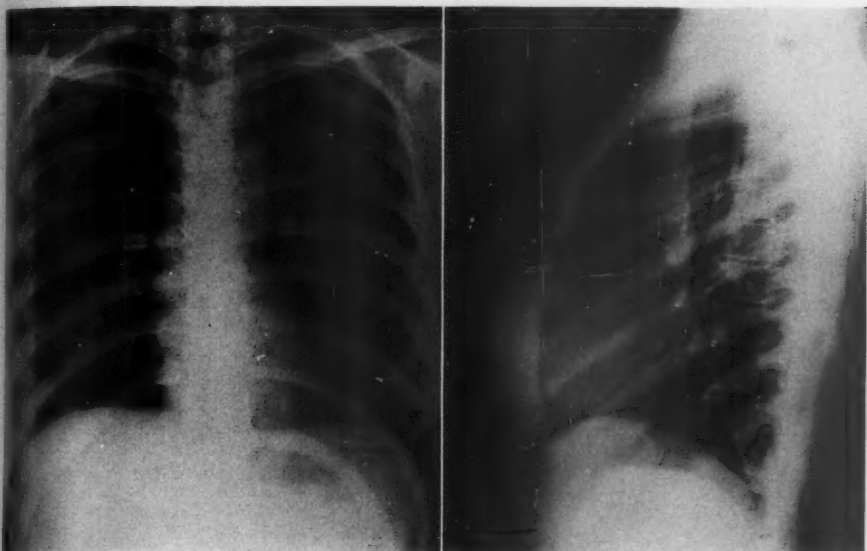


FIG. 2A. *Sarcoid*. Routine posteroanterior and lateral chest x-rays of a 26-year-old white woman who had no symptoms whatever. Skin tests were negative. At operation the left hilar mass turned out to be a mass of granulomatous lymph nodes showing the characteristic noncaseating tubercles of sarcoidosis (B). No organisms could be visualized. (From Peabody *et al.*, *J. Thor. Surg.* 35: 384, 1958.)

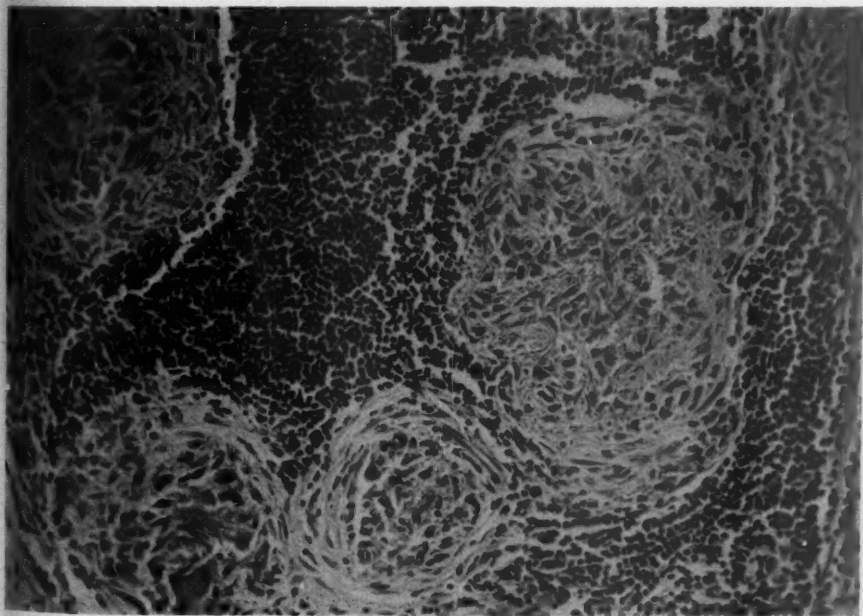


FIG. 2B, see legend figure 2A

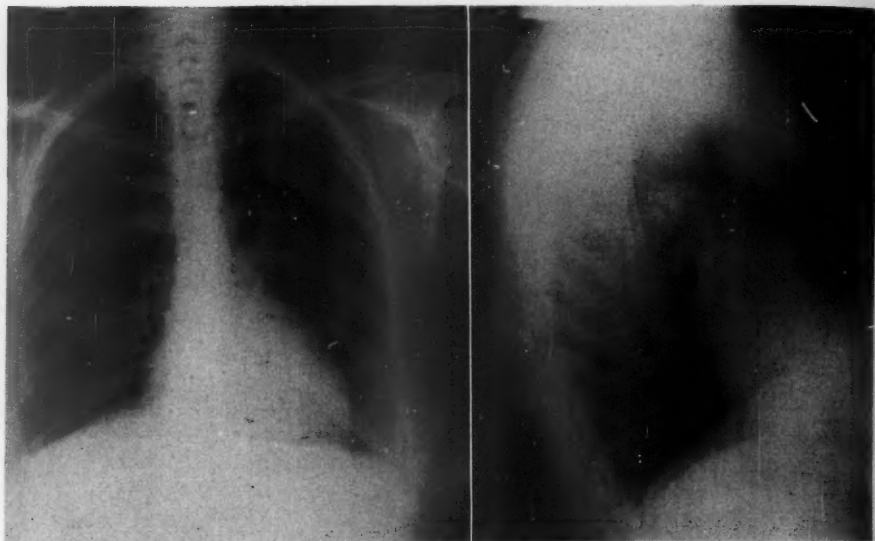


FIG. 3A. *Nonspecific lymphoid hyperplasia* in a 49-year-old white woman whose routine chest x-rays showed a right superior mediastinal mass. In the posteroanterior view it appeared as a hazy, ill defined density in the right parasternal region, but in the lateral view it looks much denser and is seen to lie immediately behind the upper sternum. At thoracotomy the lesion proved to be an ovoid anterior mediastinal tumor with reddish-brown color measuring 3 cm. in diameter (B). Microscopically, there is some resemblance to a thymoma (C), the tumor actually having been mistaken for thymoma in frozen section. Many lymphoid follicles are seen with germinal centers containing acidophilic masses in addition to the usual large reticulum cells (D). By differential staining these masses are identified as collagen.

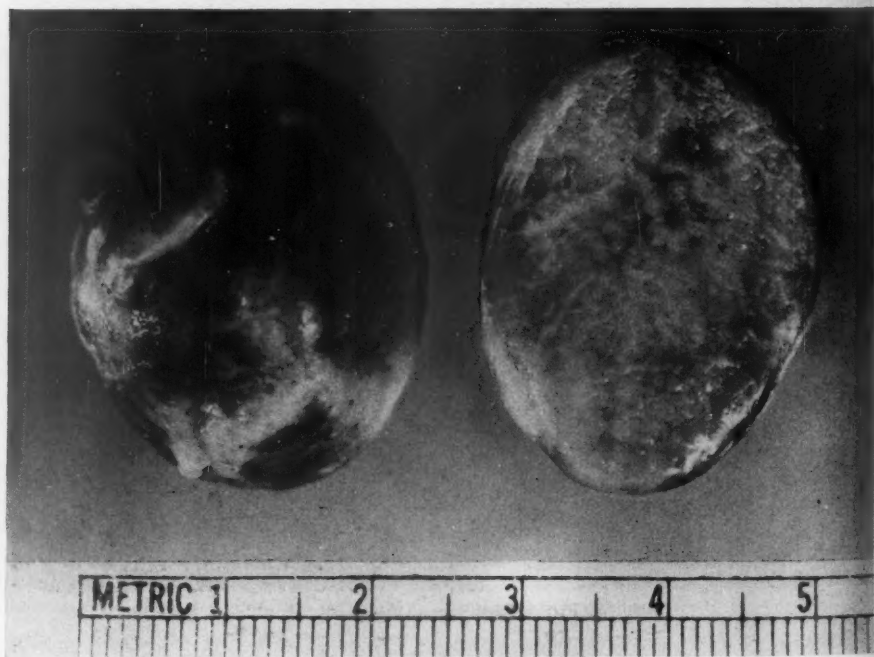


FIG. 3B, see legend figure 3A



FIG. 3C, see legend figure 3A

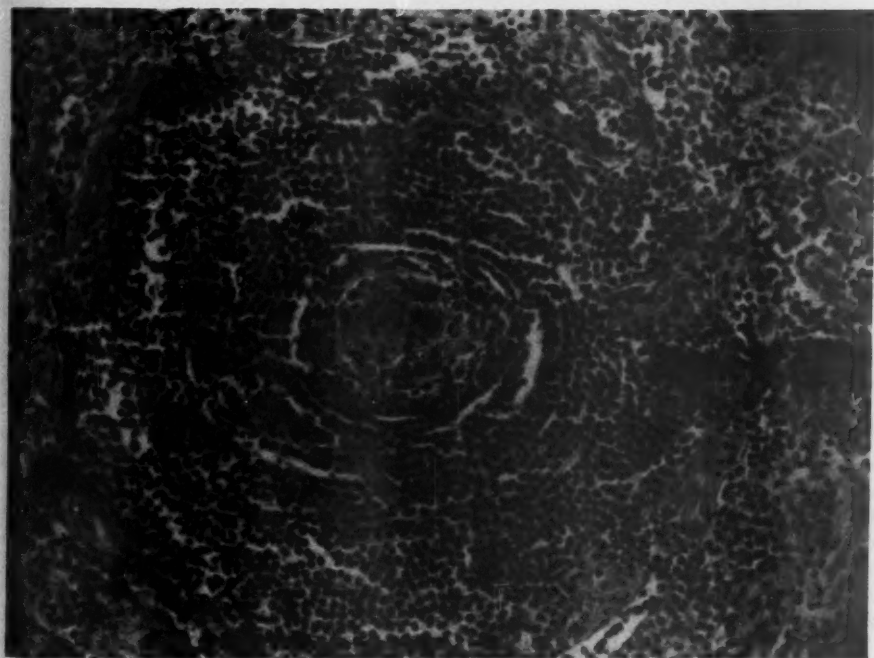


FIG. 3D, see legend figure 3A

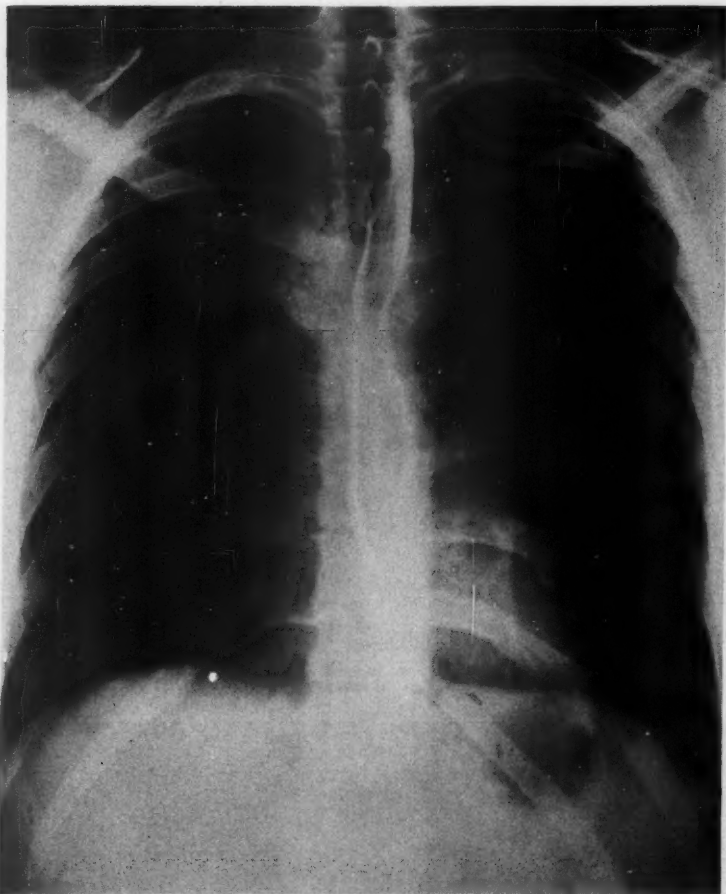


FIG. 4. A. *Histoplasma granuloma* in a 24-year-old white man, who had no symptoms related to the right paratracheal mass, first detected in routine chest x-ray. Tuberculin and histoplasmin skin tests were both positive. (A) Barium swallow showed no encroachment on the esophagus and considerable calcification could be seen within the tumor. This was misinterpreted as indicating a teratoma. At operation, a 5-cm. cystic lesion containing caseocalcific matter was excised. Originally signed out as a "tuberculoma" despite negative studies for tubercle bacilli, the lesion was subsequently re-examined and found to contain *Histoplasma* visible in both (B) periodic acid-Schiff (PAS) and (C) methenamine-silver nitrate stains.

small round calcific lesion was present in the lung parenchyma drained by the involved nodes. Occasionally calcium was also demonstrable within the mediastinal granuloma itself, giving a rather characteristic central stippled effect best brought out by overpenetrated, Bucky or tomographic techniques (fig. 4). Calcification may also take place in the rim of the lesion, where there is often no more than a thick fibrous capsule surrounding the caseous, pasty contents.

The presence of such calcium deposits within

a mediastinal tumor may strongly suggest the correct diagnosis, particularly if the lesion occupies the more or less characteristic right paratracheal position and is accompanied by a positive histoplasmin or tuberculin skin test.

An accurate diagnosis is seldom possible on radiographic grounds alone. In fact, in this series a preoperative diagnosis of granulomatous lymphadenitis was favored in just 3 cases. Lymphoma was chosen as the most likely diagnosis in 9 cases; teratoid tumor, in 4; esophageal tumor, in 2. Six



FIG. 4B, see legend figure 4A

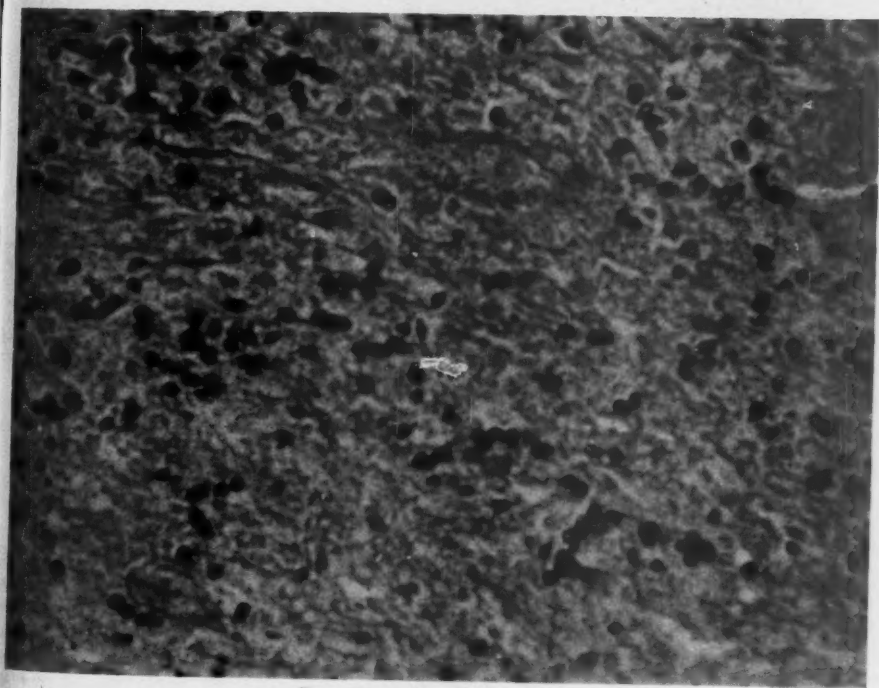


FIG. 4C, see legend figure 4A

times a no more precise diagnosis was proposed than mediastinal tumor or cyst. Other possibilities mentioned preoperatively included bronchogenic cyst, thyroid adenoma and sarcoïd.

OPERATIVE FINDINGS

With few exceptions these tumors provided a serious technical challenge to the surgeon in the form of dense adherence to surrounding structures. In some cases the margins were ill defined and appeared infiltrative, consistent with a sclerosing type of mediastinitis that precluded resection and rendered even biopsy hazardous. More often, the margin of the tumor could be delineated reasonably well, but surrounding tissue planes were obliterated by a film of fibrous adhesions to the trachea, superior vena cava, esophagus, lung root, and pericardium. Although resection was frequently difficult, it was considered the procedure of choice in most cases and was accom-

plished in this series without attendant mortality or morbidity. Several times a small portion of the fibrous capsule was left attached to vital structures (fig. 6). Once it was necessary to repair a tear in the superior vena cava and one case presenting with a superior vena cava syndrome required complete caval replacement (fig. 6). Five operations consisted solely of biopsy, usually because of the infiltrative nature of the lesion.

An awareness of this lesion and its pathologic manifestations is essential for anyone doing thoracic surgery. When encountered in the dense sclerosing form it may be mistaken for a carcinoma, while the cystic lesion filled with material resembling toothpaste is especially apt to be mislabeled a dermoid cyst. Despite their inflammatory nature these tumors need not be excised intact. Cultures of the caseous contents are rarely positive and the danger from pleural contamination is practically nil. It is sometimes wise, there-

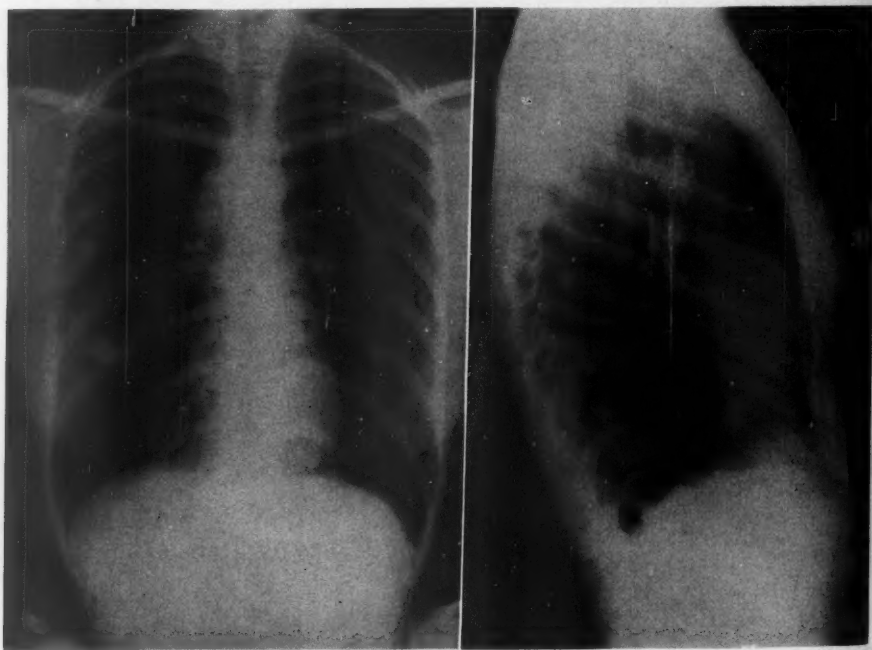


FIG. 5A. *Nonspecific granuloma obstructing superior vena cava* in a 25-year-old white female whose chief complaint was swelling of the face and neck. Chest roentgenograms showed a densely calcified mass in the right paratracheal region plus multiple parenchymal nodules of varying size, each showing consistent central calcification. Tuberculin skin test was negative; histoplasmin, strongly positive. Venogram (B) confirmed the presence of superior vena caval obstruction. Thoracotomy permitted excision of the mediastinal granuloma, thrombosed superior vena cava and a parenchymal subpleural nodule, which are seen in C. Note the puttylike contents and thick capsule of the mediastinal granuloma shown in the center. Despite the use of multiple stains and repeated study, organisms can be found neither in the mediastinal nor parenchymal component of the lesion.

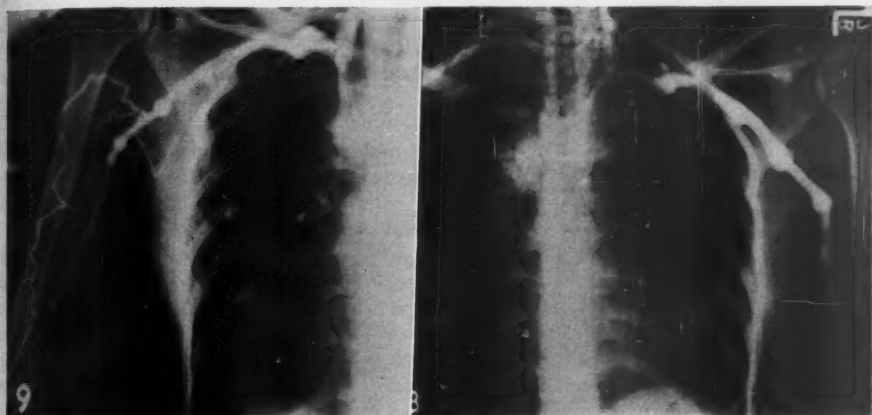


FIG. 5B, see legend figure 5A

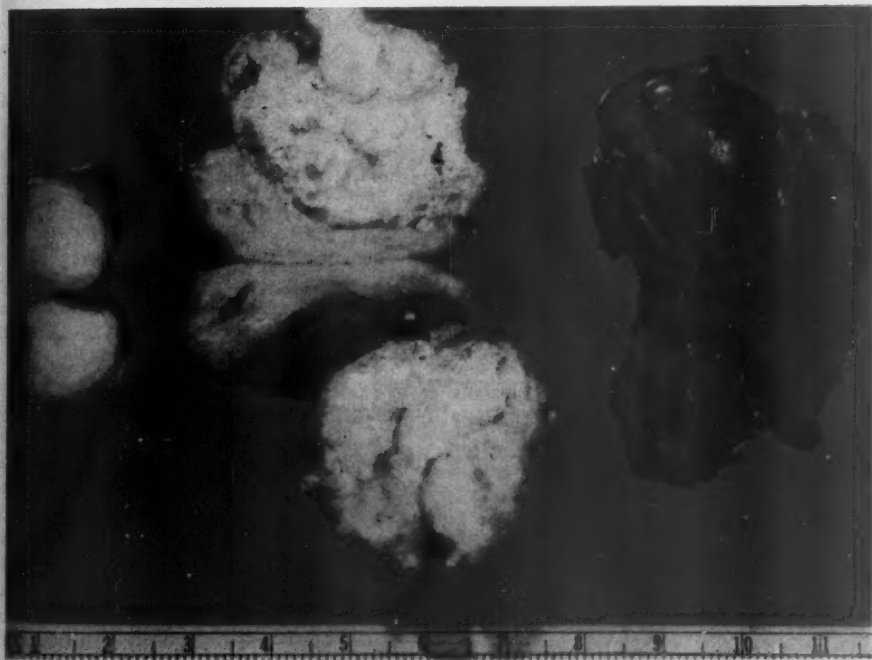


FIG. 5C, see legend figure 5A

fore, to open the cystic granuloma, evacuate its contents and leave some portion of the capsule attached to the trachea, cava or esophagus rather than invite disaster by persistent efforts to do an excision *en bloc* which ordinarily is not essential.

One helpful but often overlooked maneuver is to excise for diagnosis the small associated paren-

chymal granuloma, for this is more apt to contain microscopically demonstrable organisms than is the mediastinal component. Also, it is wise to save the "toothpaste" for fixation and microscopic study because it is here rather than in the wall of the granuloma that organisms are likely to be found.

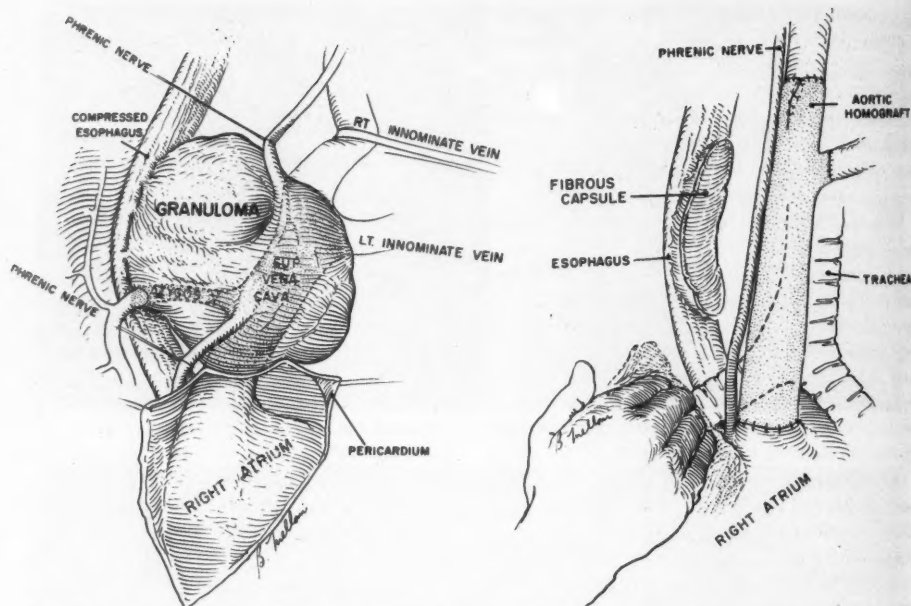


FIG. 6. Drawings illustrating the operative findings and method of treatment on the patient described in figure 5. *Left*, the typical location and densely adherent character of the granuloma can be seen; except for a portion of the capsule left attached to the esophagus, the lesion has been excised along with the thrombosed superior vena cava which it encircled. *Right*, the defect in the cava is bridged by an aortic homograft.

PATHOLOGY

From the literature one is led to believe that practically all mediastinal granulomas are unicellular cystic structures. This is not necessarily true. Eleven of our own cases (44 per cent) were solid tumors and most of these consisted primarily of dense fibrous tissue interspersed with areas of grossly granulomatous or caseous lymph nodes. A few resembled nothing more than a mass of matted lymph nodes and in an occasional case the lesion was solid without any resemblance to lymph node remaining. Fourteen granulomas (56 per cent) were cystic. One of these was multilocular. The rest were unicellular cysts measuring 4 to 6 cm. in diameter, having fibrous capsules of varying thickness and containing caseous material resembling toothpaste, cream cheese or putty. The similarity to sebaceous material has prompted the improper classification of many cases as dermoid cysts. However, there is no cellular membrane lining the cavity, the inner surface being shaggy and irregular. Microscopic examination should quickly differentiate the two.

Although the capsule was generally 4 or 5 mm. in thickness, it was extremely thin in several cases, raising the question as to whether spontaneous rupture ever occurs. Such an eventuality might explain the dense infiltrative character of the sclerosing type of granulomatous mediastinitis, but has not been documented insofar as we can determine.

Microscopically, there is considerable variation from one lesion to another. The solid tumors fall into several categories. Four lesions are consistent with the picture of Boeck's sarcoid, the normal lymphatic architecture being diffusely replaced by noncaseating granulomas (fig. 2). Epithelioid cells and giant cells are seen but caseous necrosis is notably absent. Of equal importance is the lack of any demonstrable organisms in specially stained tissue sections.

Two of the solid tumors, quite similar in microscopic appearance, bear a rather striking resemblance to a thymoma (fig. 3). Each is comprised of many lymphoid follicles with germinal centers containing acidophilic masses in addition to the

usual reticulum cells. These masses with the aid of differential staining can be identified as collagen. Lymphocytic cuffs encircle the germinal centers. Upon superficial examination, especially in frozen sections, such a tumor can easily be mistaken for a thymoma, a point emphasized by Castleman² and Iverson.⁴ In neither case can organisms be demonstrated.

A few of the solid lesions consist of very little other than large amounts of very dense collagenous connective tissue. Collections of chronic inflammatory cells may be scattered throughout the lesion along with lymphoid follicles manifesting prominent germinal centers surrounded by cuffs of lymphocytes encircled in turn by a dense mass of connective tissue. This is thought by some to deserve the term sclerosing mediastinitis. Its etiology is unknown.

Still another of the solid tumors shows prominent groups of lymphocytes surrounded by epithelioid cells encompassed by a layer of fibroblasts. With polarized light many small (1 to 3 μ) doubly refractile particles resembling silica are seen, hence its classification as a silicotic granuloma.

The rest of the solid tumors show multiple small, active tubercles with epithelioid cells, Langhans type giant cells and central caseous necrosis. In all cases a careful search was made for organisms. In no instance were acid fast bacilli demonstrated, although in one case, acid fast bacilli had supposedly been visualized in initial tissue sections. Our own reinvestigations failed to confirm this finding which we had questioned in the first place, inasmuch as the tuberculin skin test was negative in this patient. A careful search for fungi utilizing the periodic acid-Schiff (PAS) stain was likewise unrewarding. By restaining with the methenamine-silver nitrate technique of Gomori, a few scattered Histoplasma were discernible. In addition, a small granulomatous focus, excised from the middle lobe adjacent to the mediastinal granuloma, was found to contain many Histoplasma, thus emphasizing the value of excising any associated parenchymal focus as an aid in diagnosis.

The cystic types of granuloma show far less evidence of tubercle formation, their walls being composed largely of hyaline fibrous tissue and a varying number of fibrocytes. Scattered giant cells are occasionally seen, but for the most part these appear to be much older lesions and calcium

TABLE 1

Final diagnoses in 25 mediastinal granulomas

Nonspecific granuloma.....	11
Histoplasmic granuloma.....	7
Sarcoid.....	4
Tuberculous granuloma.....	2
Silicotic granuloma.....	1

deposits are quite common within the wall. The amorphous cystic contents had been lost for the most part in the process of fixation and staining of the specimen. We feel that this probably accounts for the failure in many instances to demonstrate organisms. Using the PAS and Gomori stains, Histoplasma were found in six of these cystic lesions, making a total of seven histoplasmic granulomas among the 25 cases included in this series. Acid fast bacilli were found in 1 patient, a 21-year-old white woman who manifested dysphagia and hematemesis. This was the only nonsurgical case in this series; autopsy revealed a large mass of caseocalcific nodes in the subcarinal area with ragged erosion into the esophagus.

BACTERIOLOGY

Portions of 16 specimens were cultured for tubercle bacilli. These were positive in two cases, the first described above and the other representing a positive culture from an excised scalene lymph node in a 32-year-old colored man with a typical right paratracheal mediastinal granuloma. In most of these cases, material was also cultured for fungi. The latter were consistently negative. This is no reflection on the reliability of the tissue section diagnosis of histoplasmosis, but instead probably indicates the "burnt-out" character of most of these lesions.

It has been mentioned that there was a perfect correlation between skin tests and the recovery or demonstration of organisms. The 2 patients with positive cultures for *Mycobacterium tuberculosis* had positive tuberculin skin tests; 6 of the 7 patients with histoplasmic granulomas had strongly positive histoplasmin skin tests, 1 case being tested only with tuberculin which was negative. The final diagnoses are shown in table 1.

SUMMARY

Twenty-five cases of mediastinal granuloma are reported from a total experience of approxi-

mately 200 mediastinal tumors, suggesting that this lesion is more common than is generally thought. Although any of the mediastinal lymph nodes may be involved, the typical location is the right paratracheal region in intimate apposition to the trachea and superior vena cava (64 per cent).

These lesions provide problems both in diagnosis and management. Surgery offers the only reliable approach to diagnosis and, in addition, excision represents the proper treatment in most instances. The intimate association of these granulomas with surrounding structures makes surgery hazardous, although there were no operative deaths in this series. Certain technical aids are referred to in this paper. In one instance the superior vena cava was replaced to relieve obstruction secondary to a mediastinal granuloma.

Histoplasmosis appears to be the most common single proved cause of mediastinal granulomas, accounting for seven cases. Tuberculosis should not be casually incriminated unless bacteriologic or pathologic proof is available. Various other diagnostic entities, including Boeck's sarcoid, are included in this series.

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